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VOL. XXIII FASC. 2 15 : V 1942 N:o 132

AN EXPERIMENTAL INVESTIGATION ON THE EFFECT OF ARTERIOGRAPHY WITH PERABRODIL ON THE BRAIN[1]

by

Kristian Kristiansen and *Jan Cammermeyer*

During the 10 years which have elapsed since EGAS MONIZ introduced the cerebral angiography in clinical work the method has been adopted in neuro-surgical clinics everywhere.

In the Department of Neurology, Rikshospitalet, Oslo, the first cerebral arteriography was performed in February 1938. From thence until now there has not been carried out so many examinations as might have been expected from our clinical material, only 58 arteriographies having been performed on 54 patients. The reason for the reservation shown by our department in this matter is to be found in the cases of cerebral injuries reported from various clinics since 1937, for which the contrast medium injected, viz. *thorotrast* possibly may be responsible. At the suggestion of Dr. TORKILDSEN the thorotrast was replaced by *perabrodil*.[2] According to our experiences so far this medium gives a very good contrast filling and it has not caused any complication neither in immediate connexion with the injection nor later on. As our experience on human material is restricted we have found it desirable to carry out experimental investigations with the perabrodil-arteriography on rabbits. The animals were sacrificed after a period varying from immediately up to several weeks after the injection. The whole brain was removed in one piece and examined microscopically in order to establish any contingent injury on the brain tissue or the vessel walls.

As contrast medium MONIZ used first a 25 % solution of *iodide of sodium*, but some

[1] Submitted for publication Nov. 6, 1941.

[2] According to professor T. DALE perabrodil has sometimes been used in cerebral arteriography at the Roentgen Department, Rikshospitalet Oslo, also before 1938.

From the Neurological Department of Rikshospitalet (Neurological University Clinic) at Oslo (Physician-in-chief: G. H MONRAD-KROHN, M. D. Professor of Medicine), and from the University Anatomical Institute, Oslo (Direktor: K. E. SCHREINER, M. D. Professor of Medicine).

awkward complications occurred at times, like epileptic fits and transient hemiplegies, and in 2 cases of 350 the patient died subsequent to the injection. During his search for a more suitable stuff MONIZ for a short time also used *Abrodil*, but dropped it again as, according to his statement, it did not offer any advantage to iodide of sodium. The most used medium in cerebral angiography since 1932 has been *Thorotrast*, a 25 % colloidal solution of dioxide of thorium, and both MONIZ and LÖHR, who are most experienced on these matters, maintain that the use of Thorotrast is harmless.

It may be mentioned that the American Council of Pharmacy and Chemistry as early as in 1932 emphasised that the immediate toxicity of Thorotrast was minimal, but that »the questionable point remains that of ultimate toxicity» — and the Council could *not* accept the use of Thorotrast for intravenous injections. In an editorial article in J. A. M. A., 8th May 1937, the opinion is expressed that the above-mentioned and similar materials must not be used in such a manner that they are deposited for a long time in the organism. The reason for the above warning is that Thorotrast is deposited in the system, and there it may have noxious effects because of its radio-active qualities which are mainly characterized by a rich emission of α-rays. The various authors' impression of the suitability of Thorotrast as a contrast medium is found to be greatly varying from one clinic to another. This fact is partly due to the different methods of investigation used; it is especially striking how the contingent dangers pertaining to arteriography with this medium often are dismissed neglecting necessary post-mortal examinations.

Both MONIZ, as well as LÖHR and JACOBI maintain that the arteriography with thorotrast does not involve any noteworthy risk, of immediate or ultimate complications. MONIZ, however, mentions that small colloidal particles of dioxide of thorium may stuck to the vessels endothelium, and, further, that there were often signs of »stasis of the opaque fluid in the capillaries» in the neighbourhood of tumors.

The experimental investigations with Thorotrast injections on animals have partly consisted in injections into the ventricular system or subarachnoidally, partly in injections in the cerebral parenchyma itself, and, lastly, in injections in the arterial system (arteriography). In 1934 ALEXANDER, JUNG & LYMAN published the results of their experimental investigations on dogs; they found that direct injection of Thorotrast into the cerebral parenchyma and in the cerebral ventricles produced a pure foreign-body reaction without any destructive changes which could be referred to the physicochemical nature of the material. During the following weeks the main part of the contrast medium was transported, by fagocytic cells, to the nearby blood vessels. The experience which STUCK and REEVES had derived from their subarachnoidal and intra-ventricular applications of Thorotrast on cats, dogs and monkeys, and the ensuing hydrocephalus development gave, however, reason for reflection. The last authors found that all contrast mediums when injected according to their methods, were deposited intra-cranially or intra-spinally, and they warned against the like use of Thorotrast on man. There are hardly many who share the view of FREEMAN, SCHOENFELD & MOORE who maintain that Thorotrast is a quite innocent material which may with advantage be used as an intra-ventricular contrast medium.

When Thorotrast is injected intra-vascularly (intra-venously or intra-arterially) it becomes fixed in the spleen, liver and bone marrow (KADRNKA, ROSSIER, OKA, RADT). Part of it is also recovered from lungs, placenta, and suprarenal glands (KADRNKA, ROSSIER). JUNET & KADRNKA have discovered that Thorotrast is transported through the vascular endothelium of the liver and is fixed for a time in the Kupfferian cells before it is deposited in the regional glands via the lymphatics. The experiments of WEN & JUNG showed that the reticulo-endothelial cells are not »blocked» by the thorium. NAEGELI & LAUCHE have followed the destiny of Thorotrast in dogs which they observed during several years after the injection. The last of the animals which survived the

injection of Thorotrast for 5 years, and which had also been operated upon for the sake of liver and spleen biopsy, showed at autopsy that as time had passed both liver and spleen had contained decreasing amounts of Thorotrast; the final deposit of the material had occurred in the retroperitoneal and the mesenteric lymphatic glands which had partly become quite necrotic and were enclosed in a solid capsule of connective tissue. Any excretion of the contrast medium from the organism had apparently not taken place.

ROUSSY, OBERLING & GUÉRIN provoked sarcoma in rats by means of intra-peritoneal injections of Thorotrast. On the other hand they never saw any sarcoma in the liver or spleen where considerable amounts of the material is deposited. These authors, therefore, thought it improbable that Thorotrast, when intra-venously injected, could give rise to sarcoma. SELBIE was able to confirm the development of sarcoma in rats, even though he used much smaller doses than the first-mentioned investigators did. If the observation period, therefore, can be sufficiently prolonged, we cannot exclude the possibility of a development of malignant tumors also in man.

Dangerous and even fatal consequences have been reported in many cases after limb arteriography on persons suffering from vascular diseases or perhaps from beginning gangrene, but it seems as if Thorotrast, when used for this purpose, is among the least dangerous contrast mediums (LAMBRET, LERICHE, WERTHEIMER & FRICK, MATHIEU). One can hardly blame Thorotrast for the complications caused by the technical procedure (LÖHR, FISCHER & SUNDER-PLASSMANN, MACKH). The percutaneous arteriography (SHIMIDZU, WOLFF & SCHALTENBRAND) may perhaps be of advantage in the latter respect.

Among pathological-anatomical investigations carried out on human material on which cerebral arteriography has been performed with Thorotrast, one must specially mention works by NORDMANN, by NORTHFIELD & RUSSELL, and, lastly, the large material collected at Olivecrona's clinic and published by EKSTRØM & LINDGREN. From these investigations it is rather clear that Thorotrast may produce thrombosis and embolism in the neighbourhood of cerebral tumors and abscesses, but the injurious effect may also be observed remote from the tumor. Attention should here also be drawn to the degenerative alterations of the vascular endothelium after intra-vascular injection of Thorotrast, which have been described by EFSKIND and perhaps may be a predisposing factor. BODECHTEL & DØRING state that they have found similar changes to those mentioned by EKSTRØM and LINDGREN in patients with cerebral tumor on whom arteriography had *not* been performed beforehand. (!)

In 1939 MACKH recorded 2 fatal cases after arteriography with Thorotrast, death occurred 12 hours after the injection. With a view to finding remnants of Thorotrast both the arteriographed hemispheres were chemically examined, no trace of this material, however, was to be found in the brains. Both MACKH, and now this year DYES maintain that Thorotrast is very well suited for cerebral angiography and that the risk is small compared with the advantages obtained.

DEGKWITZ's work on colloids containing iodine has recently lead to the production of an ethylated ester of triiodostearic acid (ethyltriiodostearate). DØRING, HÄMMERLI & HÄUSSLER have found no detrimental effect from this material when using it for injection in test animals, and from 1937 it has been used in clinical work, partly for hepatolienography (BECKERMANN & POPKEN), and partly for cerebral angiography (HÄUSSLER). The stuff is excreted from the organism in about 3 days. According to an information from SCHALTENBRAND to DYES, however, the medium, when injected percutaneously in the carotid artery, sometimes causes strong pains of some days' duration at the site of injection. This locally irritating effect is perhaps not without importance. Slight rises in temperature and transient indisposition have not been regarded as any important objection to the use of the material. We have not had any opportunity of trying the above material in cerebral angiography.

Perabrodil is a 3.5-diiodo-4-pyridon-N-acetate of dietanolamine and contains about 50 % fixed iodine; it is very stable in an aquous solution. It is thus not a colloidal suspension like Thorotrast and ethyltriiodostearate. Perabrodil is obtainable both in a 35 % solution and in 50 % (Perabrodil forte). After intravenous injection it is excreted through the kidneys in a few hours. It is at present the most commonly used medium for contrast filling of the urinary ducts and it has proved itself very suitable for this purpose. Perabrodil and similar bodies have previously been used in arteriography of the peripheral arteries (the arteries of the limbs). In 1934 DEMEL reported the favourable effect of arteriography with Uroselectan and Abrodil when performed on patients suffering from advanced arterial diseases. He stated that after arteriography at least one third of the entire number of patients treated showed decreased pains and the contingently commencing gangrene was stopped. It may be difficult to explain the improved circulatory conditions; SCHÜLLER regarded an irritative effect of the hypertonic salt solution to be the main factor. In 1937 DEMEL & SGALITZER described their further experiences on arteriography of the limbs; they had now changed to a 20 % solution of Perabrodil and had seen favourable therapeutical effect in 36 % of the patients arteriographed. The tests carried out on animals seemed to indicate that Abrodil and Perabrodil when injected in the arteries give rise to prolonged and distinct expansion of the finer arterial branches. French authors, however, have published several cases of arteriography where an iodine-containing medium similar to Abrodil — Ténébryl — has been used, and after which a number of serious complications — partly fatal — have ensued. (LEVEUF, DESPLAS & REBOUL, SÉNÈQUE & BENOÎT, BAZY & REBOUL, — all these authors used Ténébryl — LECLERC (Uroselectan)). LERICHE maintains that if the patient is suffering from gangrene, imminent gangrene, or from arterial diseases, iodine-containing contrast mediums must never be employed in arteriography. He had used Thorotrast in 146 cases without any serious consequences, there had only been one patient who had shown a transient complication.

CONTIADÉS, NAULLEAU & UNGAR have in an experimental and clinical work dating from 1935, çarried out comparative investigations on Perabrodil, Thorotrast, Uroselectan, and Ténébryl. They arrived at the conclusion that Perabrodil 35 % was the least injurious medium as it gives the smallest amount of vasomotoric phenomenons. The arterial endothelium proved to be quite intact even after a prolonged contact with perabrodil. The above authors performed 70 peripheral arteriographies with Thorotrast and Perabrodil on human beings without any noxious consequences, but they warn against Thorotrast on account of its radioactivity and its fixation in the organism. BAZY, REBOUL &

RACINE also prefer the organic iodine compounds for arteriographic use and mention that they have never seen any symptoms of iodism, and likewise never seen any endarterial lesion.

JUNGMICHEL was once called to do a judiciary post-mortem in a case of death after an intravenous injection of Perabrodil; he then emitted an enquiry to the various hospitals in Germany asking for information whether similar cases had been observed elsewhere. At all these clinics there had since 1932 occurred 5 deaths, 8 serious reactions and several slighter reactions, after 81.000 intravenous injections of Perabrodil. All the complications seemed to have been caused by hypersensitiveness to iodine, and the author suggested certain precautions to eliminate this danger. The experiences of other investigators seem to indicate that Perabrodil is a quite innocent body. CASTELLANOS, PEREIRAS & GARCIA have injected Perabrodil in quantitties of 12—15 c. cm. during $1^1/_2$—2 seconds only, on new-born children without descovering any complications, and ROBB & STEINBERG have injected 25—45 c. cm., 70 % Perabrodil intravenously during 2 seconds on altogether 238 grown-up patients without any consequences but a peculiar taste in the mouth, a sensation of heat in the face, head, perineum, or lower limbs, and a reddening of the skin. v. BRAUNBEHRENS reckons with a mortality figure of 1 per 50.000 after intravenous pyelography with Perabrodil, and considers that an allergic reaction is not to be entirely avoided, even if all possible precautions are observed.

If all the obtained experiences on the above mentioned contrast mediums are summarized it seems evident that so far one has not succeeded in finding the ideal compound — that is a compound which does not entail the slightest danger of serious complications in connexion with injection in the organism (the experiences on ethyltriiodostearate are still too scarce to allow any final judgment). Perabrodil is relatively harmless and it is possible that the serious allergic reactions may be evaded through a testing or a minute questioning of the patient before the examination. Since TORKILDSEN introduced Perabrodil in cerebral angiography at the Neurological Department of Rikshospitalet (Oslo), no certain noxious consequences which may be traced back to the material injected, has been observed. Such a clinical estimate is of modified value as these patients as a rule show so many neurological symptoms that new lesions may possibly remain hidden by the symptoms of the preexisting disease for example, a brain tumor; and the collection of human material for anatomical examination would take a considerable time because, in this country, angiography has so far not been used so frequently that a representative material on the subject is at hand. We, therefore, thought it desirable to obtain, experimentally, some information on the possible dangerous effects of Perabrodil. On account of extraordinary circums-

tances the present work is both belated as well as considerably shortened, but we feel entitled to publish our results so far.

The setting of the *problem* is suggested above. Our *aim* was simply to establish the presence of possible transient or lasting changes in the vascular walls, and possible perivascular derangements during, or as a result of, the Perabrodil injection.

Our Own Experiments

As test animals grown-up rabbits from different litters and races were used, 26 in all. The common carotid artery was laid bare during ether narcosis just below the mandibular angle. During this operation KRAUSE's Rabbit Atlas was used for orientation. The rabbits have no bifurcation in the general sense, as the internal carotid springs out like a small branch far up on the medial side of the ascending branch of the mandible. The rabbit's head was placed above the roentgen film and the injection needle, fastened to a syringe, was thrust into the artery. It proved necessary to apply an artery wall ligature just centrally to the place of injection as the artery wall is very thin and is unable to stop the bleeding by contraction of the muscular layer after the needle has been extracted. The Perabrodil solution was injected, and a roentgen picture was made when about one half of the syringe had been emptied. In nearly all cases a ligature had to be made just peripherally to the place of injection after the needle had been extracted, this also to prevent bleeding. *In no case did even bilateral ligatures of the carotids cause any lasting neurological defects or pareses.*

After varying intervals the animals were re-operated upon and new arteriographies were performed on the other side. This was done to save animals, and we took it for granted that in case there should be any morphological alterations, it would be possible to distinguish between old and new ones, the intervals were accordingly always made wide. The animals were thereafter decapitated during ether narcosis. After 1—3 hours the brain was dissected free and fixed either in Bouin fluid or in 10 % formalin, and after about one week it was dehydrated in the usual way. During this process the brain was kept for about 2—3 weeks in 96 % alcohol. In most of the cases a longitudinal section through the left hemisphere was made before dehydration — as a bearingpoint later on in the mounted section —, the brain was thereafter divided into 8 to 11 frontal slices which were subsequently embedded in paraffin. Sections from each block were stained with thionin and hematoxylin-eosin.

The results obtained may be reviewed as follows: —

The anæsthetic used was ether, but several animals succumbed during the narcosis before the injection of Perabrodil (Nos. 9, 16 & 21),

or shortly after the operation (no. 18). Several also showed respiratory trouble (Nos. 10 & 16), so that the ether narcosis had to be administered very carefully. On the other hand, a too superficial narcosis involved that the animals became restless or were awaked by the injection (Nos. 14 & 19).

In most of the cases bleeding occurred, partly during the injection, partly at the moment the needle was extracted (Nos. 5, 6, 7, 17 & 19); the bleeding was stopped by ligatures above and below the place of injection.

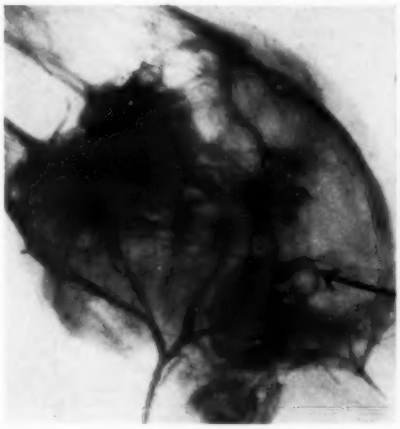
During the injection homolateral pupillary changes were often observed. Nystagmus was often seen in conjunction with the narcosis. A contraction of the pupil occurred at the injection of Perabrodil (Nos. 1, 18 (both times), 23 & 25), and pupillary dilation took place after Thorotrast and Urotrast injections (Nos. 11 & 12 respectively). After Urotrast the dilation was long-lasting (one hour) and was accompanied by a slight nystagmus (effect of the narcosis?). No. 10 turned cyanotic during the injection, and No. 7 had convulsions in the homolateral limbs. All these symptoms were, however, transient and *in no case did the arteriography leave any lasting neurological defects, pareses, or similar disturbances.*

The roentgenograms were successful in the following cases (— Nos. 8 (left) 10 (l.), 11, 12, 13, 16 (p. m.), 17 (r.), 18, 19, 23, 24, 25, 26; this gives the following *time intervals* between injection and death (intervals are calculated for each side separately in cases of bilateral injections): — *11 hours, 16 h., 21 h., 40 h., 48 h., 115 3/4 h., 8 days, 9 d., 10 d., 16 d., 32 2/3 d., & 48 d.* The results after 48 hours and 16 days are based on the examination of two animals. If in addition to these also those cases are taken into consideration in which arteriography was probable and doubtful or uncertain, namely in cases Nos. 1, 6 (r.), 10 (r.), 17 ($1._1$), and 22, as well as Nos. 6 (l.), and 17 ($1._2$), the following time intervals are added: — *less than 1 hour, 18 h., 21 h., 66 h., and 20 days, — and 42 hours and 20 days.* It seems reasonable to include these doubtful cases as it must be remembered that where so small doses and somewhat difficult experimental test conditions are concerned, a premature roentgen exposure may easily occur. We had a strong impression of the correctness of the above reflection when reviewing case No. 5 (1/4 hour interval). — When the Perabrodil was injected periarterially, partly because of bleedings, and partly because the point of the needle perforated the artery wall so that the contrast medium became deposited round the artery we naturally counted the results obtained as negative, although it is not impossible even in these cases, that a smaller portion of the material may have reached the brain. For the above reason some of the cases cannot be taken into consideration, *viz.*: — Nos. 7, 8 (r.), 14 & 15.

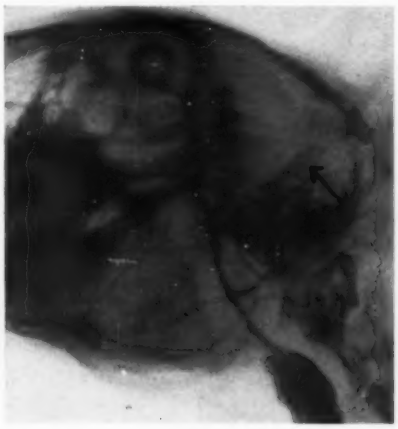
Table 1

Nos	Weight in Kilogrammes	Side	Arteriographed	Death	Time in hours (days)	Contrast Medium %	Dosis	Fixation	Roentgen	Anat.	Notes
1	1.0	R.	27/2 40	27/2	0	35	1.2	Bouin	+(?)	÷	Respiration stopped.
2	4.0	R.	29/2 »	29/2	0	50	1.0	»	÷	÷	
5	2.0	L.	14/3 »	14/3	1/4	50	0.5	»	÷	÷	Roentgen exposure too early?
6	2.0	L.	4/7 »	6/7	42	35	0.5	»	÷ (?)	÷	
		R.	5/7 »		18	35	1.0		+(?)		
7	3.0	R.	10/7 »	19/7	66	50	1.0	»	÷	?	Both times periarterial injection.
		L.	17/7 »		42	50	1.0	»	÷		
8	2.0	R.	25/7 »	31/7	139¾	50	1.0	»	÷	÷ (?)	Periarterial injection.
		L.	26/7 »		115¾	50	1.5		+		
10	1.0	L.	27/9 »	1/11	32¾ d.	50	2.0	»	+	÷	25/10 40: 2 c. cm. 35 %. Perabrodil in auricular vein.
		R.	29/10 »		66	50	2.0	»	+(?)		
11	1.1	L.	15/10 »	17/10	48	Th.	2.0	»	+	÷	
12	3.5	L. 1	31/10 »	16/11	16 d.	50	2.0		÷ (?)	÷ (?)	
		2				50	4.0	»	+		
		R.	7/11 »		9 d.	Th.	2.0		+		
13	3.0	L.	13/11 »	31/12	48 d.	Th.	2.5	Formal	+	÷	
		R.	21/11 »		40 d.	Th.	3.0		+		
14	1.0	L.	25/11 »	5/12	10 d.	Ut.	3.0	»	÷	÷	Periarterial injection. Transient anisochoria and nystagmus.
15	2.5	L.	9/12 »	10/12	10 d.	50		»	÷	?	Periarterial inj.
		R.	10/12 »		ca. 72	50		»	÷		Periarterial inj. Spontaneous death. Sepsis?
16	3.0	L.	17/1 41	17/1	0	35	4.5	»	+	÷ (?)	Death from narcosis. P. m. inj.
17	2.5	L. 1	24/1 »		20 d.	50	1.5		+(?)		
		2				50	1.0		÷(?)		
		R. 1		13/2		50	3.0	»	sl.+	÷	
		2	28/1 »		16 d.	50	1.0		sl.+		
		3				50	3.0				Partly periarterial inj.
18	2.0	L.	4/2 »	12/2	8 d.	50	2.0	»	+		4/2 41: Cortex lesion of the right side.
		R.	12/2 »		0	50	2.0		+		Respiration stopped after 45 min.
19	3.0	L. 1	27/2 »	1/3	ca. 48	50	0.5	»	+		17/2 41: Lesion of the left hemisphere.
		2				50	2.0				
21	1.8			4/4							Death from narcosis.
22	2.0	L.	4/4 »	5/4	21	35	2.0	»	+(?)	÷	
23	2.0	L.	7/4 »	9/4	16	50	2.0	»	+	÷	
24	2.3	L.	7/4 »	8/4	21	50	2.1	»	+	÷	
25	2.5	L.	17/4 »	18/4	11	50	1.5	»	+	÷	
26	3.0	L.	17/4 »	19/4	40	50	3.2	»	+	÷	

Nos. 3 & 4 were rabbits which had been used for other purposes, and post-mortally injected with cinnabar-gelatin and dissected to investigate the course of the arteries. No. 9 died during the narcosis and was thrown away. No. 20 died some hours after an operation during which a piece of bone wax had been introduced subdurally to try to imitate the effect of a cerebral tumor. »R.» and »L.» in the column »Side» give information on which side the carotid injections and ligatures were performed. The numbers after the letters in some cases, indicate that repeated injections were made on the same



1.



2.

3

Fig. 1. Rabbit No. 3.
Post-mortal injection with cinnabargelatin to illustrate the vessel system in the head. Ramifications from internal carotid at (◂—). Even when filled with this very dense contrast medium the finer arteries of the brain do not show.

Fig. 2. Rabbit No. 10.
Some Perabrodil periarterially at the place of injection. Ramifications from internal carotid at (◂—).

Fig. 3. Rabbit No. 11.
Thorotrast. Slight, but distinct filling of the arterial system.

side during the same operation, a new puncture being made just above the previous ligature; this was especially done if the first roentgenogram was unsatisfactory. »Contrast Medium %» gives the strength of Perabrodil used. »Th.» indicates Thorotrast. »Ut.» means Urotrast, i. e. Perabrodil manufactured by Nyco (Norwegian). »+(?)» or »÷(?)» means probable filling or doubtful filling. »Sl.» means slight contrast. In the column Anat.» »?» indicates that in case No. 7 there was a definite meningitis, and in No. 15 there was a very intense meningoencephalitis. »(?)» indicates a moderate amount of lymphocytes in the meninges or in the brain.

Further — see the text.

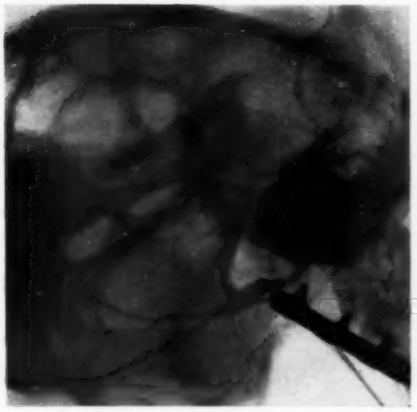


Fig. 4. Rabbit No. 12.
Perabrodil; good filling.

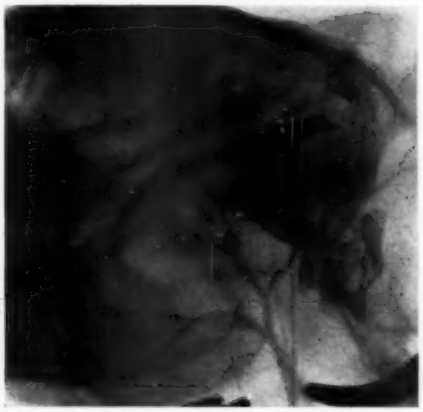


Fig. 5. Rabbit No. 16.
Dead from narcosis. Post mortal injection. Good filling, but even here no visible arterial branches intra-cranially.

Among the roentgenograms we have selected a few which illustrate the rabbit's arteriogram. Fig. 1 shows a post-mortal arteriography with a very strongly contrast giving cinnabar-gelatin substance. Even on this roentgenogram nothing can be seen of the cerebral arteries, except the first branching off of the internal carotid which appears as a small fan-like collection of vessels, whereas the further ramifications are too narrow to show roentgenologically. At dissections of brains which had previously been arteriographed with cinnabar-gelatin, we found a very distinct filling in the arteries all over the brain of the intense red substance which is an excellent medium to distinguish with the naked eye the finer vessel branches. We, accordingly, feel entitled to draw the following conclusion: — When there is an equally good filling of Perabrodil or Thorotrast in the large arterial trunks in the rabbit's head, the arteries of the brain must also be filled with the contrast medium even if it is not possible to follow the finer branches roentgenologically because of their inferior calibre.

The other 4 illustrations show the looks of successful arteriograms with Perabrodil and Thorotrast. (The contrast obtained with Thorotrast in Fig. 3, however, is somewhat more scarce than usual, probably on account of an exposure ill-timed to the injection. — classified in table 1. with + mark).

The anatomic investigations of all animals with successful and more or less successful arteriograms, did not disclose any traceable changes (see table 1.).

As control animals for the anatomical examination we had to use rabbits dead of respiratory paralysis during narcosis. Furthermore, we made use of the not-injected side of the brain for comparison. We would mention, however, that this latter method is not quite reliable — because there will also in the rabbits be plenty of anastomoses between the two hemispheres, and Perabrodil may also, to a certain extent, be distributed

all ove r the brain via the arterial circle of Willis. We do not know the conditions in the rabbit's brain in this respect, but if a paralellism may be drawn between the latter and the human brain it is not probable that any substantial amount of contrast would pass to the contralateral hemisphere. It is quite a different matter that, in conformity with the conditions in men (conf. MONIZ and LÖHR), we may obtain fillings also of the other side's hemispheric vessels if cinnabar-gelatin is injected post-mortally on control animals.

We would next like to say a few words about the histo-anatomical examination. In all regions the nerve-cells showed the general aspect: — A round nucleus, poor in chromatin, with a distinct nuclear membrane and a dark, approximately centrally sited nucleole. Especially on the convexities the cortical nerve-cells were somewhat pale of colour and some of them had a vacuolised cytoplasm. Groups, or more extensive areas, of very dark and shrunken nerve-cells were found to be evenly distributed in both hemispheres. In no sections could there be detected any distinct disappearance of nerve-cells which might indicate that the dark and shrunken forms should be pre-stages of irreversibly damaged cells. The shrunken cells were most often found in the deeper layers of the cortex, on the convexity as well as basially. It lies near, therefore to refer them to cell forms described by SCHARRER as arising through pressure on non-fixed cerebral tissue. A feature which also goes to show the same is that the pericellular space is not widened. Nerve-cell changes of the type »Primäre Reizung» were found in case No. 8 in the medulla oblongata on the one side, but this was probably due to a lesion on one of the cerebral nerves (n. vagus?) at the operation on the neck. — In the cerebellum there were numerous heterotopies of the Purkinje cells in the molecular layer.

No hypertrophy or hyperplasia was seen of either microglia, astroglia or oligodendroglia. Here we had to give attention to the fact that the astroglia nuclei of the first cortical layer and in the medulla may often have a quite large vesicular nucleus. Likewise, numerous partly confluent groups of oligodendroglia nuclei were seen near the ventricular system. There were no signs of gliosis or cytoplasmic hypertrophy of the astroglia. The vessels were next very carefully examined both with regard to the endothelial nuclei and to the various elements of the walls; but in no case could any traceable changes be found. In all sections there was a perivascular space intersected by fine fibres.

The endothelial cells of the vessels were slightly »swollen» in most of the sections, and had a nucleus which bulged a trifle into the lumen; this was, however, the general aspect in nearly all the cases and no significance could be attached to it. There were no thrombi; and in the lumen of the vessels there were no corpuscular elements at all which could be

stained. This also applied even to those rabbits to which Thorotrast had been administered. Blood and serum of an ordinary appearance filled the lumen, but at the same time there was often a distinct vacuole formation along the periphery. In nearly all cases, moreover, there were fresh red blood corpuscles in the leptomeninges and in the ventricles. There was no phagocytosis of blood pigment in the brain or in the meninges, but in the latter there were some melanotic pigments (especially in No. 12). There were no morbid signs to be traced in the ependyma and the choroid plexus.

In two of the rabbits (Nos. 7 & 15) a considerable inflammatory reaction had developed. In No. 7 the lymphocytes and plasma cells were restricted chiefly to the meninges, but were also found around the smaller vessels in the upper cortical layer. There was also a small perivascular microglia nodule in the medulla oblongata. In case No. 15 the infiltration of lymphocytes and plasma cells was very massive and intense, and it was also mixed up with numerous macrophages. In this same case there was also a diffuse glia reaction in the subpial cortex and perivascularly round the vessels in the cortex, and even far into the white matter. Further, in the cortex of both hemispheres there were numerous granulomata, about the size of one field of vision at 200 times' magnification. These granulomata were composed by numerous scavenger cells round a strongly dilated vein. Most of the scavenger cells seemed to be restricted to the Robin-Virchows space, and round this space there was a denser brim consisting of microglia and hypertrophied astroglia, diffusedly spreading into the brain. The vessels just outside were surrounded by numerous lymphocytes and plasma cells and some scavenger cells. Some of the nerve-cells, especially those along the deeper layers, showed pathological changes which resembled ischæmic homogenisation. In rabbit No. 12 there was a moderate infiltration of lymphocytes in the leptomeninges and around some of the cortical capillaries. In No. 8 there were also a few sporadic lymphocytes in the leptomeninges. Finally, in rabbit No. 16 there was a small perivascular brim of lymphocytes on the ventral surface of the frontal lobe. In No. 18 there appeared to be a small lesion of the cortex and an ensuing decrease of nerve-cells together with an atrophy of the cortex. Around this necrosis there was a slight glia reaction and a hypertrophy of microglia and astroglia nuclei. In rabbit No. 19 a large lesion of the brain was found which, in a small area, stretched as far inwards as to the lateral ventricle; corresponding to this there was, in the walls on the opposite side, a small fibrous intra-ependymal nodule, full of vessels. Around the cortical lesion there was a considerable hypertrophy and increase of the astroglia and microglia, as well as some degenerated and »pale», tigrolytic nerve-cells and thick-walled vessels. The lesion was sited on the convex surface about 2 millimeters from the

median line, and near the middle of the hemisphere in fronto-occipital direction. Below this necrosis, and nearly quite separated from it, however, a pseudolaminar »zone of reaction» was found in the 5th- 6th cortical layers stretching from the frontal pole and nearly as far as the occipital pole. The number of cells in this zone was considerably increased, mostly because of the highly increased number of scavenger cells round the vessels, the endothelial nuclei of which were somewhat swollen and also increased in number. Moreover, some lymphocytes and plasma cells were situated round about the vessels. Numerous hypertrophied astroglia cells containing much cytoplasm, were diffusedly spread in the cortex. The same astroglia reaction was present, though not equally intensive, all the way through the cortex up to the surface. It was not possible to determine whether there had occurred any decrease of nerve-cells, neither might any definitely pathological forms be ascertained. In the rearmost part of this pseudolaminar zone there were numerous large perivascular lymphocytical infiltrates all the way up to the surface of the cortex. In the leptomeninges on the opposite side there was a small perivascular brim of lymphocytes. In the thalamus of the same side there appeared a pronounced »paling» of the lateral nucleus and a decrease of the nerve-cells which partly seemed swollen and pale, and showed an excentrically displaced nucleus (retrograde change!).

Discussions

In two cases a partly intense meningoencephalitis was ascertained. With regard to the time interval we saw several other cases having the same intervals, but showing no morphological changes. There is thus no correlation between the inflammatory state and the time factor. It was also roentgenologically established that most of the Perabrodil was deposited round the place of puncture and for this reason there is little probability that the inflammation reaction should be due to the material injected. In one of the two cases mentioned (*viz.* No. 15), there were secretions from both ears already before the first arteriography, and the meningoencephalitis may thus have been caused by a sepsis with septic embolism to the brain. Finally, it must be taken into consideration that meningoencephalitis is very easily provoked in rabbits. In our special investigations we were fortunate enough to be able to exclude both cases beforehand because the injections were periarterial. It next lies near to consider the possibility that Perabrodil might perhaps decrease the immuno-biological reactions of defence, as observed and described with regard to Thorotrast (HANKE). This did not seem to be quite correct, however, where the Perabrodil was concerned in our investigations; No. 14 was, for example, quite negative even after 10 days of observation.

It must be admitted that in rabbit No. 8 a few sporadic lymphocytes were noted. In rabbit No. 12 there was a moderate lymphocytic meningitis which must probably also be regarded as not specific. The observations regarding No. 16 also seemed to point in the same direction; in this case Perabrodil was injected post-mortally, and one single small perivascular lymphocytic infiltration was histologically found in the orbital region.

Next, there were two rabbits on which a brain lesion was brought about before the arteriography was performed (No. 19), or simultaneously (contralaterally in No. 18), for the purpose partly to decide whether the Perabrodil would have any damaging effect on vessels which had been lesioned beforehand, and partly whether it would influence the morphological aspect of the lesion. These investigations must, of course, be further supplemented, and our observations so far are much too summary to allow any final conclusion as yet. We should also like to use methods which would decide the activity of the »blood-brain barrier», *inter alia versus* microbial embolism (conf. TORE BROMAN). NORDMANN's investigations have shown, according to TORE BROMAN, that Thorotrast has a noxious influence on the blood-brain barrier. Contrary to Thorotrast, however, Perabrodil is neither radio-active nor a colloidal body, and it is possible that it has no injurious effect on the vessels. During our investigations concerning Perabrodil we have found no support for the hypothesis that this material should bring about any decrease in the resistance of the blood-brain barrier. No perivascular oedema was found, nor were there any recent or older hæmorrhages which could be traced back to the effect of Perabrodil, nor any limited necrosis. With regard to the two animals on which a necrosis in the brain was called forth at the operation, there was no exceptional changes in the brain in the one case in which a simultaneous contralateral arteriography had been performed; in the second case with homolateral arteriography there was, 10 days after the brain had been damaged, beside the limited lesion, an extensive pseudolaminar area with numerous hypertrophical glia cells as well as perivascular infiltrations. The above picture displaying a mixture of ectodermal and mesenchymal reactions, appears somewhat extraordinary. For the moment, however, it is impossible to put it down to the Perabrodil's account. The problems raising out of these investigations, as well as experiments on the decrease of the blood-brain barrier, and imitation of »tumors» by the introduction of wax globules, must be elucidated through further research work. With regard to animal No. 19, which had a pseudolaminar zone of reaction of mixed type, the changes in this zone and in the cortical lesion were of the same kind (called forth simultaneously?), and were probably in both places due to either the surgical trauma, the ether narcosis, or the carotid ligature (?). The reason

for the lack of a clear functional defect of the nerve-cells is probably due to the small intensity of the ischæmia (conf. SPIELMEYER), and only the glia system has thus been activated. A similar, mixed aspect with numerous infiltrations due to inflammations has, moreover, been described, in connexion with spontaneous epilepsy with amaurosis in apes, by VAN BOGAERT & H.-J. SCHERER, and in human beings by JANSEN, KÖRNYEY and SAETHRE.

Further, all rabbits which had been injected with Perabrodil, were negative with regard to possible histological changes in the brain, when examined according to the usual methods (Thionin and hematoxylin-eosin stainings).

In this connexion it is remarkable to note that Thorotrast has also given a similar negative result, in accordance with the statement by BODECHTEL & WICHMANN, but this is in opposition to the pathological experiences on man, obtained by WERTHEIMER & FRICK, NORDMANN, NORTHFIELD & RUSSELL and by EKSTRÖM & LINDGREN. It may be possible that this divergency is conditioned by peculiarities in the material examined. It may also have its cause in the size of the material examined, — even in EKSTRÖM & LINDGREN's large material there are many negative cases. We must also take a similar possibility into consideration in our small Perabrodil-treated material. Even though the present paper must, therefore, be looked upon as a preliminary report only which necessitates further studies, it is clear that the composition of Perabrodil and its rapid excretion (conf. intravenous urography), makes it unlikely that this material should possess the same characteristics as Thorotrast. We hold it likely that even compared with the recommended colloidal ethyltriiodostearate, Perabrodil, which is soluble in water, would appear to be the more advantageous. Continued control experiments and clinical experience will, however, also in this question be of decisive importance.

Nearly all cases presented fresh bleedings in the meninges and in the ventricles. These findings are probably attributable to the manner in which the animals were killed, and the brain removed, because there was no histological finding which would seem to indicate that these bleedings had any connexion with the Perabrodil arteriography.

Finally it should be mentioned that Perabrodil has not done any damage in any way to the brain, when repeated injections on the same side have been performed. By the kind suggestion of Professor THJØTTA (Bacteriological Institute, Oslo), we have in one case tried to establish whether an allergic reaction developed. Perabrodil was injected in an ear-vein about one month after the first arteriography (No. 10). When a new contralateral arteriography was performed 4 days later, no reaction of neither clinical nor histological nature was observed. — Repeated contralateral arteriographies with intervals of from 2—10 days never

caused any noxious reaction. In this connexion it should be considered whether the amount of Perabrodil used, *viz.* up to 4 c. cm., might call forth an anoxæmia in the brain. Rabbit No. 12 which had been given the above dose just after a dosis of 2 c. cm. in the homolateral common carotid artery, showed no morphological signs of any such effect. We have not here ventured to estimate the real amounts which may have penetrated into the brain. If the doses given to the rabbits are put to comparison with those used on man, 2—4 c. cm. is, after all, a very considerable dose for a rabbit. The ramification of the arteries, however, is so different in rabbit and in man, that the whole dosis of Perabrodil injected cannot get into the rabbit's cerebral capillaries as it may in man. All these matters taken into consideration, it is possible, all the same, that Perabrodil, when injected, may cause a displacement of blood over a long distance because of the small diameter of the arteries in the rabbit's brain. It may also perhaps be possible that the simultaneous carotid ligature may contribute to the augmented anoxæmia-producing effect of this column of fluid, because, under the circumstances, the Perabrodil cannot be expected to mix with the blood at once as it would do when blood circulation in the artery was intact. During our investigations we have found no support for the assumption that Perabrodil should be able to cause any such local anoxæmia. This particular point will, of course, also have to be subjected to special investigation after closing of the branches from the common carotid artery, with the exception of the internal carotid, and exclusion of other factors which may also lead to ischæmic processes (*inter alia* carotid ligature and ether narcosis), etc. With regard to the carotid ligature, all the »pure» Perabrodil cases have shown that even this operation on rabbits need not lead to any morphological changes.

We have not examined the condition of the other organs. Through investigations carried out by JUNET and KADRNKA, and others, we know that Thorotrast becomes deposited in the spleen and liver. This, however, will probably not apply neither to Perabrodil nor to the ethyltriiodostearate, because these latter bodies are so quickly excreted through the kidneys.

SUMMARY

To study the effect of Perabrodil on vessels and nerve-tissue more closely, experimental arteriographies of the carotid area in rabbits have been carried out. In 17 arteriographies on 13 animals in all the roentgenological control disclosed a good filling of the arterial system, whereas there were doubtful fillings 8 times in 6 animals. After varying time intervals — from less than 1 hours up to 48 days — the rabbits were killed and neuro-anatomical examinations were performed. In a few cases in which, moreover, the arteriography was unsuccessful, a state of inflammation was observed; this latter may probably be explained by the often occurring spontaneous encephalitis in rabbits. The brains of all the rabbits which were examined after a successful arteriography with Per-

abrodil, showed no pathological changes of either the vessel walls, nerve-cells, or glial tissues. Nor was there any evident noxious effect of the Perabrodil in or about the lesioned area in two rabbits on which the hemisphere had been injured before performance of arteriography.

ZUSAMMENFASSUNG

Um die Wirkung des Perabrodil auf Gefässe und Nervengewebe näher zu untersuchen, haben die Verff. experimentelle Arteriographien aus dem Carotisgebiete an Kaninchen vorgenommen. Röntgenologische Kontrolle zeigte Füllung des Arteriensystems bei insgesamt 17 Arteriographien an 13 Tieren, während die Füllung achtmal an 6 Tieren zweifelhaft war. Die Kaninchen wurden später nach verschiedenen, von weniger als einer Stunde bis auf 48 Tage wechselnden Zeitintervallen geschlachtet und neuroanatomischer Untersuchung unterworfen. In einigen wenigen Fällen, wo die Arteriographie übrigens misslungen war, wurde ein Entzündungszustand wahrgenommen, der sich wahrscheinlich durch den häufig bei Kaninchen vorkommenden Spontanencefalitis erklären lässt. Sämtliche Kaninchengehirne, die nach wohlgelungener Arteriographie mit Perabrodil untersucht wurden, zeigten keine patologischen Veränderungen an Gefässwänden, Nervenzellen oder Gliagewebe. In ein paar Fällen, wo vor der Arteriographie eine Läsion der Hemisphäre vorgenommen war, fand man auch keine schädliche Wirkung des Perabrodils in dem lädierten Teil oder in der Umgebung desselben.

RÉSUMÉ

Afin d'étudier de plus près l' action du »Perabrodil» sur les vaisseaux et sur le tissu nerveux, les auteurs ont fait des artériographies carotidiennes expérimentales sur des lapins.

Le contrôle radiologique le la visibilité des artères cérébrales a donné les resultats suivants: bonne visibilité en 17 artériographies sur 13 animaux, visibilité incertaine en 8 artériographies sur 6 animaux.

Les animaux ont été tués après moins d'une heure jusqu'à 48 jours et les cerveaux ont fait l'objet d'un examen neuro-anatomique. Dans un petit nombre de cas, où, d'ailleurs, l'artériographie n'a pas réussi, on a trouvé un état d'inflammation dans le cerveau, probablement due à l'encéphalite spontanée assez fréquente chez le lapin.

Dans tous les cas où l'artériographie à »Perabrodil» a réussi l'on n'a pas mis en évidence aucune signe d'action délétère sur les vaisseaux, sur les cellules nerveuses ou sur la névroglie.

En deux cas, où une lésion expérimentelle d'une hémisphère cérébrale a été faite avant l'artériographie, on n'a pas, non plus, trouvé d'action nuisible du »Perabrodil» à l'examen de la partie lésée ou de ses environs.

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AUS DER RÖNTGENABTEILUNG DER UNIVERSITÄTSKLINIK IN UPPSALA
(CHEF: PROFESSOR H. LAURELL)

FLÜSSIGES FETT IM KNIEGELENK NACH TRAUMA[1]

von

Bengt S. Holmgren

Dass sich bei intraartikulären Frakturen flüssiges Fett in der Gelenkhöhle findet, ist den Chirurgen wohlbekannt. Unter anderen haben HOLM und HULTÉN darauf hingewiesen, dass man bei Kniegelenkfrakturen mit Erguss im Gelenk Fett im Punktat in einer Menge bis zu 10 % nachweisen kann. Der Amerikaner KLING hat 15 Fälle von Knieverletzungen mit Erguss im Gelenk zusammengestellt und Fett im Gelenkpunktat sowohl bei intraartikulären Frakturen als bei Verletzungen der Ligamenta cruciata und bei Meniscusverletzungen konstatiert. In den positiven Fällen war das Punktat immer zugleich hämorrhagisch.

1939 wurde auf der hiesigen Röntgenabteilung flüssiges Fett in einem Kniegelenk bei intraartikulärer Tibiafraktur festgestellt. Der Befund beruhte auf einer ausnahmsweisen Änderung der gewöhnlich befolgten Technik. Weil Pat. nicht auf der Seite liegen konnte, wurde das Seitenbild des Kniegelenks (Bei Rückenlage des Patienten) mit horizontaler, statt mit vertikaler Strahlenrichtung aufgenommen. Auf dem Bilde sah man an der Stelle der Bursa suprapatellaris unter dem Musculus quadriceps und seiner Sehne einen Schatten, der weniger dicht war als der Schatten dieser Gewebe. Die Dichte entsprach ungefähr der von Fettgewebe. Unter dem »Fettschatten» war ein flüssigkeitsdichter Schatten mit oberer horizontaler Abgrenzung gegen das Fett sichtbar. Die Grenze zwischen den genannten Flüssigkeiten war scharf. Man sah ein deutliches Niveau zwischen Fett und Blut in der Gelenkhöhle. Auf andere Weise konnte das Bild nicht gedeutet werden. Beide Flüssigkeiten waren also aus dem Knochenmark durch den intra-artikulären Spalt in die Gelenkhöhle eingedrungen. Ein gleichartiges Flüssigkeitsniveau (Blutniveau[2]) war auch

[1] Bei der Red. am 22. XI. 1941 eingegangen.

[2] In der Folge wird statt Blutniveau der nicht ganz zutreffende Ausdruck Fettniveau gebraucht, weil uns hier das Fett, nicht das Blut, interessiert.

in dem kephalen Teil der Gelenkhöhle selbst zu bemerken (siehe Bild 1).[1] Dieses lag etwas höher, und die Grenze zwischen den Niveaus wurde durch die unvollständige Scheidewand markiert, die sich normalerweise oft zwischen der eigentlichen Gelenkhöhle und der Bursa suprapatellaris befindet. Das genannte Septum ragte in das darüber liegende Fett hinein und war deshalb als ein positiver Schatten sichtbar. Es bildete offenbar bei Rückenlage eine Schwelle für das Blut, die schwerere dieser geschichteten Flüssigkeiten. Bei Punktion des Gelenks wurde die Diagnose bestätigt.

Im Hinblick auf diesen Fall wurden später alle intraartikulären Kniegelenksfrakturen mit horizontaler Strahlenrichtung photographiert, um grössere Kenntnis von der Häufigkeit solcher Fettniveaus zu erlangen. Auch eine Reihe andere Knieverletzungen wurden in gleicher Weise unter Nachforschen nach diesem Symptom photographiert. Anfangs wurden die Bilder mit einem Fokus-Film-Abstand von 70 cm aufgenommen. Bei dieser Technik war jedoch die Grenzfläche zwischen dem Fett und dem Blut bisweilen nicht scharf genug, weil es schwer war, den Zentralstrahl längs dieser Fläche mit genügender Genauigkeit zu zentrieren. Bei unrichtiger Zentrierung war das Niveau mehr oder minder undeutlich — ja, es konnte manchmal ganz verschwinden. Man konnte sich leicht ausrechnen, dass die Unschärfe, welche auf solcher fehlerhafter Zentrierung beruhte, mit Vergrösserung des Fokalabstandes abnehmen musste. Deshalb gingen wir zu einem Fokus-Film-Abstand von 1.5—2 m über. Zentriert man mit dieser Technik den horizontalen Strahl auf den hinteren Teil der Basis patellae, so erhält man befriedigende Schärfe eines vorhandenen Niveaus, auch wenn dieses nicht genau in dieser Höhe liegt. Das Photographieren geschieht leicht mit einem Forssell-Stativ bei Rükkenlage des Patienten auf einer Rollbahre. Beim Durchleuchten stellt man die Bursa suprapatellaris und vorderen Teil des Kniegelenks selbst in ein horizontales, genügend abgeblendetes Strahlenbündel ein. Der Film wird nicht dicht am Knie angebracht, sondern am besten 10—15 cm von ihm entfernt, um grösseren Kontrast zu bekommen. Ein kleiner Fokus (Rotalixröhre) und der grosse Abstand zwischen Röhre und Gegenstand gewährleisten befriedigende Bildschärfe trotz des verhältnismässig grossen Abstandes zwischen Knie und Film. Mit dieser Technik, welche 1931 von LAURELL angegeben worden ist, erhält man kontrastreiche Bilder der Weichteile, um die es sich hier handelt.

Mein Material umfasst 65 Fälle von Knieverletzungen, welche in 4 Gruppen eingeteilt sind. Wo nichts anderes gesagt ist, handelt es sich um frische Traumata.

[1] Die Röntgenbilder dieses Aufsatzes sind nach einem Verfahren reproduziert, das von med. lic. A. FRANTZELL ausgearbeitet worden ist und später in Acta Radiologica veröffentlicht werden wird.

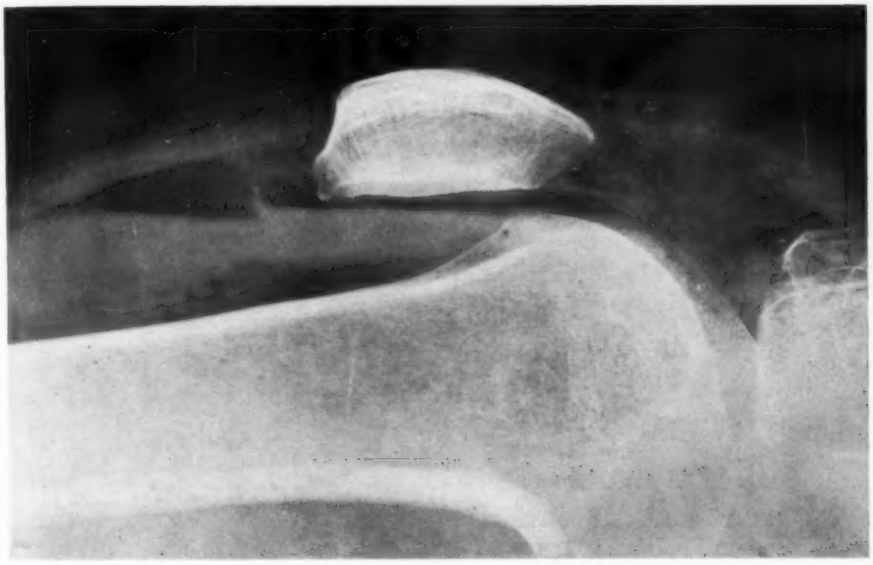
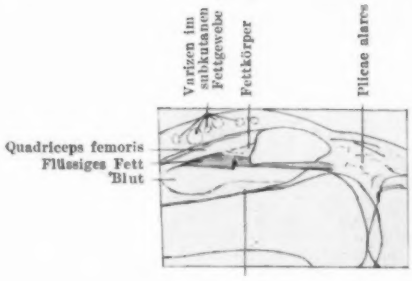


Bild 1.



I. Fettniveau bei Kniegelenksfraktur. 26 Fälle.

19 grössere Frakturen in Femur oder Tibia.

2 Fälle mit unbedeutender Herabpressung des lateralen Tibiacondylus.

2 Fälle mit Abreissung von der Eminentia intercondylica.

1 Fall mit kleiner Absprengung vom hinteren Rande des medialen Tibiacondylus.

2 Fälle von Patellarfraktur in Form von Sternfraktur mit Diastase zwischen den Fragmenten.

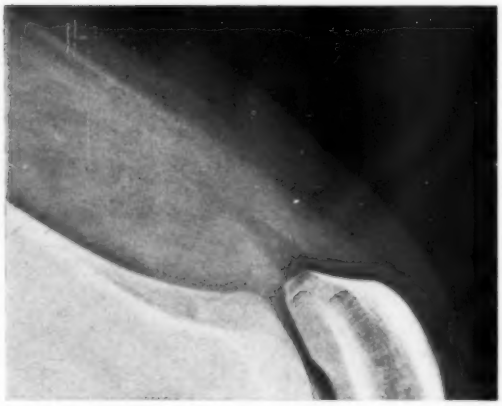


Bild 2.

II. Fettniveau ohne sichtbare Fraktur. 3 Fälle.

1 Fall von Patellarluxation.

1 Fall mit starkem Erguss in das Kniegelenk nach kräftigem Trauma.

1 Fall mit starkem Erguss in das Kniegelenk, der beim Gehen auf ebenem Boden eingetreten und von starken Schmerzen begleitet war.

III. Fraktur ohne sichtbares Fettniveau. 15 Fälle.

5 Fälle mit grösseren oder kleineren Frakturen in Femur oder Tibia.
6 Fälle von Patellarfraktur mit und
2 Fälle ohne Verlagerung der Fragmente.

Diese 11 Fälle wurden mit 70 cm Fokus-Film-Abstand photographiert.

1 Fall von Tibiafraktur mit Diastase zwischen den Fragmenten. Punktion 2 Tage nach der Verletzung zeigte Fett im Gelenk. Bei Röntgenuntersuchung 4 Tage nach der Verletzung war kein Fett nachweisbar. 2 m Fokus-Film-Abstand.

1 Fall von Tibiafraktur mit Diastase zwischen den Fragmenten. Die Röntgenuntersuchung erfolgte 14 Tage nach der Verletzung, und dabei war kein Fett im Gelenk feststellbar. 2 m Fokus-Film-Abstand.

IV. Erguss im Kniegelenk nach Trauma. Keine Fraktur noch Fettniveau sichtbar. 21 Fälle.

8 Fälle wurden mit 70 cm, 13 mit 2 m Fokus-Film-Abstand photographiert. Von diesen 13 wurden 9 punktiert. Im Punktat bemerkte man ausser Blut nur in 2 Fällen minimale Fetttröpfchen. In dem einen von diesen war der Patient nach 10, in dem andern nach 14 Tagen gesund.

Bild 3.

Es ist in der Regel nicht schwer, ein Fettniveau auf einem mit geeigneter Technik aufgenommen Röntgenbild des Kniegelenks zu erkennen. Die einzige Fehlerquelle, an die man denken muss, ist der kleine Fettkörper, der sich normaliter an der Basis der Patella zwischen der Gelenkkapsel selbst und der Sehne des Musculus quadriceps findet (siehe Bild 2). Dieses Fettgewebe kann je nach dem Fettpolster des Patienten sehr verschieden entwickelt sein und manchmal auf dem Röntgenbild fehlen. Es ist oft auf Seitenbildern des Knies sichtbar, und zwar natürlich sowohl bei horizontaler als bei vertikaler Strahlenrichtung. Man braucht es niemals mit flüssigem Fett im Kniegelenk zu verwechseln.

Bild 3 zeigt Fettniveau in einem Fall, wo man weder auf dem Frontal- noch auf dem Seitenbild eine Fraktur beobachten konnte, wohl aber einen starken Erguss im Kniegelenk. Man nahm nun ergänzende Bilder mit etwas abweichender Projektion auf, wobei eine kleine Absprengung vom hinteren Rande des medialen Tibiacondylus auf dem Seitenbild hervortrat. Von Interesse ist, dass in den oben beschriebenen Fällen trotz so unbedeutender Knochenverletzung so grosse Fettmengen ins Kniegelenk eindringen konnten.

Bei allen intraartikulären Kniegelenkfrakturen, abgesehen von Patellarfrakturen ohne Verlagerung, kann man mit der angegebenen Technik röntgenologisch flüssiges Fett im Gelenk nachweisen.

Sieht man weder auf dem Frontal- noch auf dem Seitenbild eines traumatisierten Kniegelenks eine Fraktur, wohl aber einen kräftigen Erguss im Gelenk (in der Bursa suprapatellaris), so soll man ein sog. Niveaubild aufnehmen. Findet man nun ein Fettniveau, so soll man ergänzende Bilder mit z. B. 45° Drehung des Beines und eventuell auch Stereobilder aufnehmen. Wahrscheinlich entdeckt man dann meist eine Fraktur. Kann man trotzdem keine solche bemerken, so schliesst dies ja bekanntlich

nicht mit absoluter Sicherheit eine solche aus. Es ist nämlich möglich, dass die angewandten Strahlenrichtungen nicht geeignet waren, eine unbedeutende Fissur nachzuweisen.

In dem Fall mit Patellarluxation sowie bei dem Patienten, der beim Gehen auf ebenem Boden plötzlich starke Schmerzen in dem einen Knie bekam (siehe unter II in der Tabelle), konnte ich trotz des Vorhandenseins eines Fettniveaus keine Fraktur feststellen, sondern hielt es für wahrscheinlich, dass die Plicae alares zwischen der Patella und einem der Femurcondylen geklemmt worden waren und das flüssige Fett im Kniegelenk geliefert hatten. In dem dritten Fall der Rubrik II — Fettniveau ohne sichtbare Fraktur — muss man wohl wegen des kräftigen Traumas in erster Linie eine Fissur vermuten, die auf den aufgenommenen Bildern nicht hervortrat. Hier ist auch eine vorübergehende Patellarluxation als Erklärung denkbar. Zu bemerken ist jedoch, dass nicht alle Fälle von Patellarluxation Fettniveau aufweisen; in einem Fall, der reponiert und dann sofort röntgenuntersucht wurde, war kein Fettniveau feststellbar.

Niveaubilder aufzunehmen, wenn kein deutlicher Erguss im Kniegelenk vorliegt, lohnt sich nicht. Ausserdem muss die Verletzung frisch sein, da man schon nach ein paar Tagen ein früher beobachtetes Fettniveau nicht wiederfinden kann, nicht einmal, wenn die Fettmenge ziemlich gross war. Dies beruht wahrscheinlich darauf, dass ein Teil des Fettes resorbiert wird, und möglicherweise auch darauf, dass das Blut im Gelenk teilweise kleine Gerinsel bildet, die eine deutliche Niveaubildung verhindern.

Dass das hier angewandte Photographieren mit langer Distanz der Technik mit relativ kurzem Fokus-Film-Abstand beim Nachweis von Fettniveaus überlegen ist, scheint daraus hervorzugehen, dass sämtliche Fälle von frischen Frakturen, die kein Fettniveau aufwiesen, mit der letzteren Technik photographiert wurden.

Einen merklichen Unterschied in der Heilungszeit zwischen den Fällen mit Fettniveau ohne beobachtete Fraktur und denen, wo weder Fettniveau noch Fraktur feststellbar war, konnte ich nicht finden.

Ausserdem ist darauf hinzuweisen, dass keiner dieser Fälle mit Fettniveau klinische Zeichen von Fettembolie aufwies.

Was in vielen meiner Fälle in Erstaunen setzen muss, ist, dass so grosse Mengen Fett auch bei ziemlich kleinen Frakturen in das Kniegelenk eingedrungen sind. Bei allen grösseren Frakturen werden also höchstwahrscheinlich verhältnismässig grosse Fettmengen aus dem Knochenmark freigemacht. Es ist deshalb nicht zu verwundern, dass bei einem Teil der verletzten Patienten klinische Zeichen von Fettembolie auftreten. Würden die klinischen Erscheinungen bei Fettembolie nur auf der Fettmenge beruhen, die bei der Fraktur aus dem Knochenmark freigemacht wird, so müssten solche Symptome bedeutend häufiger auf-

treten, als es der Fall ist. Für ein grosses klinisches Material (70 000 Fälle) wird die Zahl der Fälle mit tödlich verlaufener Fettembolie auf nur 1.4 ‰ angegeben. Die Fettmenge, die auf einmal in die Blutbahnen des Menschen eindringen muss, um Erscheinungen von Fettembolie (gewöhnlich schwere, lebensbedrohende) hervorzurufen, beträgt nach verschiedenen Autoren 20—30—50 g. So grosse Fettmengen werden sicher oft bei Frakturen freigemacht, ohne dass Erscheinungen von Fettembolie auftreten, weil nur ein Teil des Fettes, und dieser wahrscheinlich nicht auf einmal, in die Blutbahn gelangt. Eine grosse Menge tritt ganz sicher zusammen mit Blut in die Weichteile um die Fraktur aus, und bei intraartikulären Frakturen auch in die Gelenkhöhle.

ZUSAMMENFASSUNG

Bei so gut wie allen Fällen von intraartikulären Kniegelenkfrakturen dringt Fett aus dem Knochenmark zusammen mit Blut in das Kniegelenk ein und schichtet sich über dem Blut. Röntgenologisch kann man das Fett durch Photographieren mit horizontaler Strahlenrichtung nachweisen. Der Verfasser betont die Bedeutung dieser Erscheinung für den Nachweis kleinerer Frakturen im Kniegelenk.

SUMMARY

In practically all cases oi intra-articular fractures of the knee joint, fat from the bone marrow, together with blood, invades the knee joint and forms a layer over the blood. The fat can be shown roentgenographically if the photographing is done with the rays directed horizontally. The author stresses the importance of this sign in the diagnosis of small fractures in the knee joint.

RÉSUMÉ

Dans presque tous les cas de fracture intraarticulaire du genou une certaine quantité de graisse provenant de la moelle osseuse pénètre dans la jointure en même temps que le sang et forme une couche qui surnage sur le sang. Ou peut mettre la graisse en évidence par la radiographie en dirigeant les rayons horizontalement. L'auteur souligne l'importance de ce symptôme pour la démonstration des petites fractures du genou.

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A CASE OF DIFFUSE MYOMATOSIS AND CYST FORMATION IN THE LUNG[1]

by

Thomas Rosendal, M. D.

The case described in the following represents a pulmonary disease which, pathoanatomically, must be characterised as diffuse myomatosis and cyst formation. It is interesting because of its uncommonness, and on account of the importance of its roentgenologic picture for the diagnosis from miliary tuberculosis, Boeck's sarcoid, silicosis, miliary carcinosis, carcinomatous lymphangitis and other, similar conditions showing a diffusely small-spotted lung tracing.

Case History

The patient was a woman, born March 29th, 1889. There was no certain infcmation as to illnesses in childhood or youth; especially none as to affections of the respiratory organs. Since 1933, she had suffered in steadily increasing degree from functional dyspnea, palpitations and pains in the precordium. In 1934, she was admitted to the Bispebjerg Hospital, Dep't B, where no signs of cardiac affection were found. Later in the same year she was admitted to the Medical Dep't of the Sundby Hospital owing to intermittent attacks of dyspnea, which, however, did not resemble bronchial asthma. Roentgen examination showed some veiling of the basal portion of both lung fields. This was interpreted as indication of pulmonary stasis, and the case was diagnosed as degeneration of the myocardium. In 1940, she was again admitted to the Sundby Hospital, owing to an acute attack of dyspnea. At the same time she had a slight hemoptysis. *Roentgen examination of the lungs* (Fig. 1) now showed large, radiating hilus shadows and a diffuse, small-spotted, net-like tracing in both lung fields, most strongly pronounced distally. The reticular pattern was caused by numerous small, branching shadows, which surrounded translucent areas varying in size up to that of a pea. The roentgenograpic picture was interpreted as indicative of Boeck's sarcoid or,

[1] Reported, in 1940, at a meeting of the Danish Radiological Society, as a case of cystic lung, and in 1941, at the Northern Congress of Radiology, in Stockholm, as a case of diffuse myomatosis and cyst formation in the lung.

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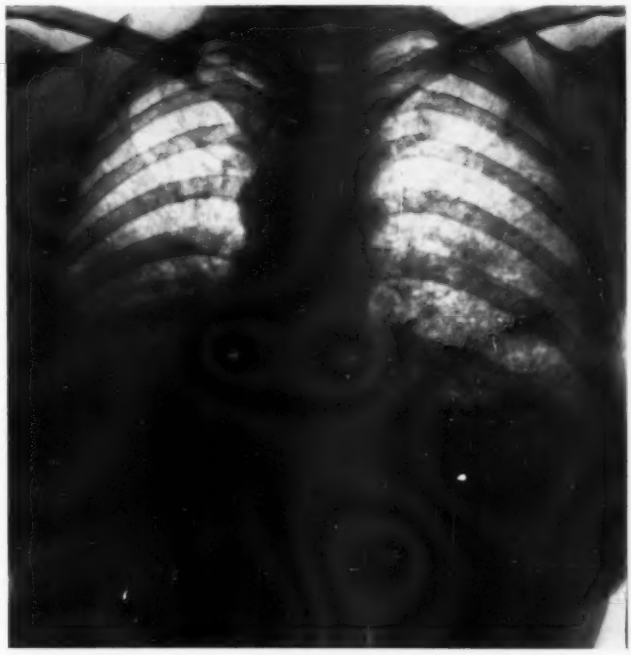

Fig. 1. Radiograph of the lung.

possibly, of miliary tuberculosis. A comparison of this roentgen finding with the one mentioned above, from 1934, shows that the changes then found in the basal portion of both lung fields, though much less pronounced, are perhaps of the same character as those in the later picture.

Examination of the patient revealed no signs of cardiac disease. On stethoscopy, coarse râles were heard at various points over both lungs. There were no tubercle bacilli in the sputum. The Wassermann reaction was negative. The temperature and urines were normal. The hemoglobin percentage 92; the sedimentation reaction 45 mm./h. There were no cutaneous or ophthalmic changes, and no lymph node swellings indicative of Boeck's sarcoid. After being confined to her bed for a month, the patient died with symptoms of respiratory insufficiency and pneumonia.

On *necropsy*, both lungs were found edematous and hyperemic. The section surfaces were in all parts of the organ deep red, carnified, with considerable increase of the interstitial tissue and with a generalised, cystic honeycomb design partly hidden by edema and hyperemia. These changes are seen more distinctly in the formalin-hardened preparation (Fig. 2). The cavities were of all sizes up to that of a pea. In various parts of both lungs there were also pneumonic foci. The trachea and

Fig. 2. Section surface of the formalin-hardened preparation.

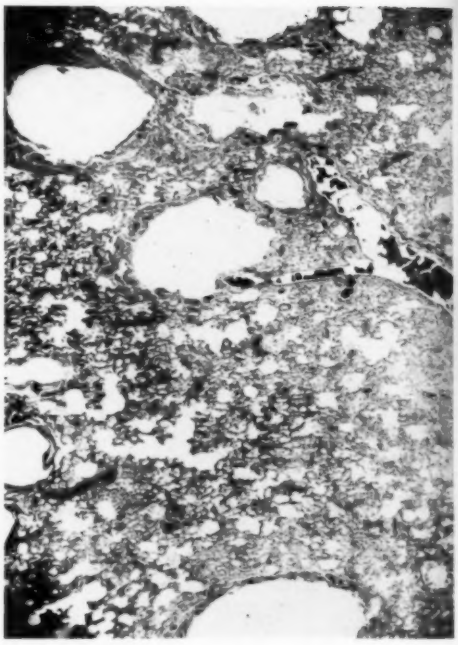

Fig. 3. Microscopic section of lung (× 12).

bronchi showed hyperemic mucosa with bloody edema in the lumen. There were no signs of bronchiectasis formations. The lymph nodes about the hilus and in the posterior and retroperitoneal parts of the mediastinum were enlarged and succulent. Both pleuræ were diffusely, fibrously thickened; most so in the right side, where the two pleural layers and the lobes were fused together. The heart, the aorta and the large vessels showed nothing abnormal. The other organs showed nothing of interest; it is especially to be noted that there were no focal changes either in the brain, the liver, the spleen or the kidneys.

Microscopy of various sections of the lung tissue showed (Figs. 3, 4 and 5) a general transformation characterised by dilatation in various degree of the alveoles and bronchioles, up to the size of millet-seeds and peas. Many of the cavities contained desquamated epithelium and, here and there, cardiopathic cells and edematous fluid; but there were hardly

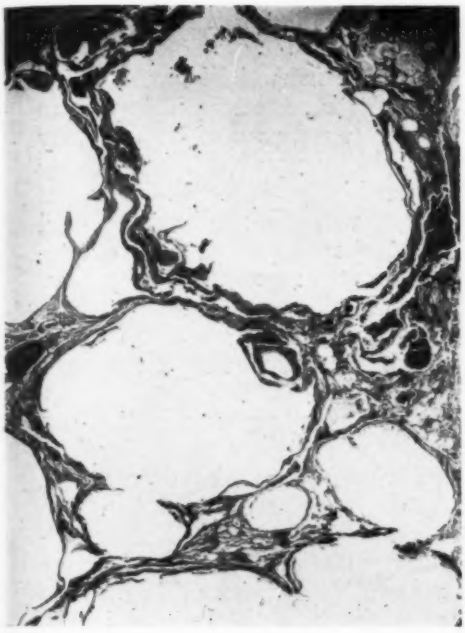

Fig. 4. Microscopic section of lung (× 75).

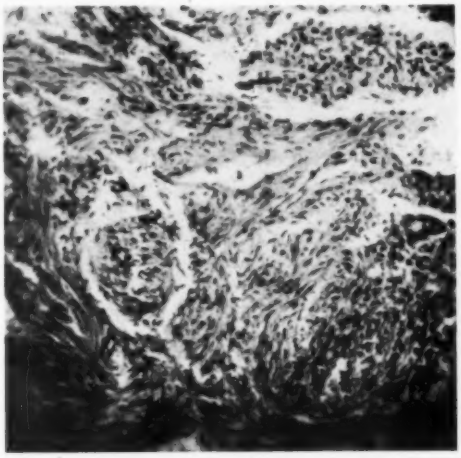

Fig. 5. Microscopic section of lung (× 200).

any inflammation products. In a few places there were smaller areas with normally dimensioned or less ectatic alveoles. The enlarged alveolar cavities were separated either by solid septa rich in cells or by septa which also contained more or less normal or atelectatic alveoles, in the walls of which the highly cellular stroma either lost itself or was entirely absent. The solid septa were built up of homogeneous, highly cellular tissue composed of bundles and streaks of slender, medium-sized fusiform cells with oblong, oval or rod-shaped nuclei. The cells were uniform, without mitoses or any difference in the size of the nuclei, and stained yellow when treated ad modum Van Gieson. Between the cell bundles there were small quantities of collagenic, in places slightly hyalinised, connective tissue. The cells closely resembled the proliferating cells seen in the growth centres of a myoma. In the interstitial tissue there was also hemoglobinogenic and anthracotic pigment. Here and there about the bronchioles there was inflammatory infiltration. Microscopy of lymph nodes from the hilus and mediastinum showed that the lymphatic tissue had become replaced by the same kind of slightly differentiated, smooth muscle cells.

The hypophysis was large, with abundant representation of basophile and eosinophile cells.

In view of the considerable increase of the interstitial tissue, which is composed of muscle cells of normal structure, the histologic picture of the lungs just described must be characterised as a diffuse, slightly heterogeneous, myomatous change of the pulmonary tissue, surrounding alveobronchiolic cavities for the greater part highly distended. In several places, the muscle cells lie in direct contact with the medium-sized and smaller, blood-filled vessels, which in many parts are relatively dominating in the tissue. It is possible that the diffuse myomatosis may have arisen from such vessels; still, the changes described cannot be characterised as angiomyomatous. That the changes should have been derived from nerve tissue is on all accounts unlikely, considering the manner of staining and disposition of the cells.

Taking the case history, the results of the roentgen examination and the necropsy findings together, we thus have here the case of a patient who for a number of years has been suffering in increasing degree from respiratory insufficience, presumed to be due to a cardiac affection. The result of the roentgen examination of the lungs points to a diffuse affection of the interstitial tissue. The necropsy discloses a diffuse increase of the latter and a, likewise diffuse, small-cystic dilatation of the alveoles and bronchioles. Microscopy shows that the interstitial tissue in the lungs and the lymph nodes in the hilus and mediastinum are for the greater part composed of smooth muscle; and, pathoanatomically, the affection must be characterised as *diffuse myomatosis of the lungs and the corresponding lymph nodes*, with diffuse *transformation of the alveoles and bronchioles into small cysts*.

Similar cases have been described in 1937 by VON STOESSEL, in 1939 by BERG and VEJLENS, and in 1941 by BERG and ZACHRISSON.[1]

In one of VON STOESSEL's cases, the patient, a man aged 51, had for many years suffered from respiratory insufficiency with dyspnea, coughs and cyanosis; in the other, the patient, a woman aged 43, had had the same symptoms for a year. She had at some previous time had dry pleurisy of the left side and had been an inmate of a sanatorium for tuberculous diseases. In both these patients, the roentgen examination of the lungs showed enlargement of the hilus shadows and a diffuse, smallspotted design in both lung fields. In the woman there was, besides, spontaneous pneumothorax in the left side. On necropsy, the lung surfaces were in both cases found of a »hobnailed» appearance, as in

[1] Since the present was written, two more cases of the same pulmonary changes have been reported, respectively by DE FINE LICHT and by SAMUELSEN, at a meeting of the Danish Radiological Society, in 1941.

cirrhosis of the liver. All sections of the lungs showed considerable increase of the interstitial tissue and diffuse cystic dilatation of the alveoles and bronchioles. The section surfaces presented exactly the same appearance as seen in Fig. 2. Besides, there were subpleural bubbles of emphysema, pneumothorax of the left side, chronic lymphadenitis of the hilar and tracheal lymph nodes, hypertrophy of the right side of the heart and chronic stasis in the abdominal organs. Microscopy showed in every part of the interstitial tissue of the lungs an enormous accumulation of smooth muscle in bundles and streaks; of connective tissue, in several places hyalinised; and, finally, cystic dilatation of alveoles and bronchioles.

In BERG and VEJLENS's case, a woman aged 32, the disease began with spontaneous pneumothorax, whereupon there developed an increasing respiratory insufficience, which eventuated in death two years later. The patient had, besides, sebaceous adenoma (Pringle's nevi) in the face and subungual fibromas of fingers and toes. Roentgen examination of the lungs and necropsy showed precisely the same changes as described above. The necropsy further revealed tuberous sclerosis of the brain; numerous small tumors, composed of embryonal, smooth muscle, in the kidneys; and in the spleen a tumor, the size of a hen's egg, composed of reticulum cells (splenoma). Microscopy of the lung tissue showed diffuse myomatosis.

In one of the cases described by BERG and ZACHRISSON, the patient, who was 30 years old and a sister of the above-named, likewise had sebaceous adenoma and subungual fibromas, had suffered from dyspnea for a year and presented exactly the same roentgenologic changes in the lungs. In the anterior wall of her vagina there was found a tumor the size of a man's fist, which after extirpation proved to be a myoma of embryonal character. Ophthalmoscopy revealed in the fundus of the eye a tumor half the size of the papilla of the optic nerve, like that occurring in tuberous sclerosis.

In BERG and ZACHRISSON's second case, a man aged 30, the disease began with left-side spontaneous pneumothorax. The roentgen examination of the lungs showed conditions similar to those described above. There were no clinical signs of tuberous sclerosis. Neither in this nor in the preceding case did bronchiography reveal any communication between the bronchial system and the small cystic formations in the lung.

VON STOESSEL regards the disease as a »muscular cirrhosis» with degeneration of the lung parenchyma and localisation of the pathological process to the supporting tissue. He bases this conception on the consideration that a chronic inflammatory condition in the lungs, especially in the interstitial tissue and the walls of the bronchioles, must be the primary element. The term: cirrhosis of the lung was first used by BUHL, in

1872, to denote a chronic pneumonia with so great an accumulation of connective tissue in the interstitial tissue that the alveoles and bronchioles become shut off and compressed. VON STOESSEL cites a number of authors who have demonstrated the occurrence of smooth muscle in the interstitial tissue in cases of chronic pneumonia, syphilis, pneumostasis, bronchiectasis and cystic lung. He adds, however, that in many of these cases the »muscular cirrhosis» was not, as in his own two cases, a diffuse generalised process and the principal disease, but only an incidental finding, showing itself as circumscribed changes. He does not think that the smooth muscle cells are disposed in a manner characteristic for myoma, and believes that they have developed by proliferation from a subepithelial, embryonal layer in the alveoles and bronchioles.

Against VON STOESSEL'S conception of the disease as being due to a primary inflammatory condition it may be argued that in the cases reported no chronic, inflammatory changes have been demostrated in the lungs. Moreover, there is nothing in any of the various case records to indicate the previous existence of such a condition in the organ. In the case which I am reporting here, and which I began by describing, the disease commenced with dyspnea, and the bronchial symptoms did not show themselves until late in its course. In two of the cases reported from elsewhere, the disease began with spontaneous pneumothorax, and the generalised process in the lungs became manifest immediately afterwards by the roentgen examination. Only in one case is there a record of left-sided pleurisy in the anamnesis.

It also seems doubtful whether there is any analogy between the localised occurrence of smooth muscle in the lung which several investigators have demonstrated in pulmonary diseases arisen on the basis of an inflammation, and the occurrence of such muscle tissue in all parts of the organ in the cases which we are discussing.

When it is argued that the smooth musculature cannot be indicative of myoma formation owing to its reticular disposition about the distended alveolar cavities, there is this to be said, that, on the contrary, such a net-like structure is bound to result from the circumstance that the process is localised to the air-filled lung tissue with its cystic cavities. That the smooth muscle is disposed in bundles and streaks must in fact be said to be characteristic precisely for a myomatous process. Those are also the criteria on which BERG and VEJLENS base their classification of the pathologic process.

A peculiar feature of the case reported by BERG and VEJLENS and of the first of those described by BERG and ZACHRISSON is the simultaneous occurrence of tuberous sclerosis of the brain, the cutaneous changes similar to those seen in the latter disease, and the tumor formations in the kidney, spleen, vagina and retina. BERG and VEJLENS point out that

tuberous sclerosis is sometimes seen in connexion with tumors of smooth muscle in various organs. They believe that the occurrence of the smooth musculature in the lungs must be considered as such a tumor formation and that both diseases may be due to some congenital disturbance of the endocrine system. That the last should be the case is rendered less probable, however, by the fact that in none of the six cases mentioned did symptoms of the disease appear until after the thirtieth year of age. In my own case, the roentgen examinations of the lungs from 1934 and 1940 showed that the disease had progressed, and this, too, speaks against the supposition of a congenital malformation.

From all that has been said here it will be seen that the etiology of these cases is doubtful, and that nothing certain can be said about the pathogenesis of the disease. If we compare my own case with those which I have cited from the literature, there is reason to point to the great similarity in the case history, which is characterised by the same increasing respiratory insufficiency and spontaneous pneumothorax with which the disease began in two of the six of the latter, and which in four of them was found by roentgen examination or necropsy. Also the roentgen findings in the lungs are precisely the same in all the six cases. The same is true of the pathologic condition in that organ which was demonstrated at necropsy in four of the cases, and which must be characterised as one of diffuse myomatosis together with a — supposedly secondary — transformation of alveoles and bronchioles into small cysts.

As mentioned, the disease in two of the cases began with spontaneous pneumothorax, presumably owing to rupture of subpleurally situated alveolar cavities. This suggests the advisability of examining all patients with spontaneous pneumothorax with a view to the pulmonary disease here described, and perhaps in this way some further light might also incidentally be shed on the problems which it is still presenting. Finally, it must be pointed out that the roentgenologic changes in the lungs observed in these cases — the diffuse, reticular, small-spotted design — are found also in a number of other pulmonary affections (see the beginning of this paper), and it is not improbable that there among these might be demonstrated hitherto wrongly interpreted cases of the disease which has been the subject of this report.

SUMMMARY

The author reports a case which clinically was characterised by increasing respiratory insufficience during a number of years. The roentgen examination showed a general increase of the interstitial tissue of the lung, and the necropsy, corresponding to this, diffuse myomatosis of this tissue, of the hilar and mediastinal lymph nodes, and a general cystic dilatation of the alveoles and bronchioles. The case is compared with 5 cases reported in the literature, in which precisely similar changes in the lungs are described, and in two of which there was tuberous sclerosis at the same time.

ZUSAMMENFASSUNG

Verf. berichtet über einen Fall, der klinisch durch zunehmende respiratorische Insuffizienz während einer Reihe von Jahren charakterisiert war. Die Röntgenuntersuchung zeigte allgemeine Vermehrung des interstitiellen Gewebes der Lunge und die Obduktion in Übereinstimmung hiermit eine diffuse Myomatose dieses Gewebes, der hilaren und mediastinalen Lymphknoten sowie eine allgemeine zystische Dilatation der Alveolen und Bronchiolen. Der Fall wird mit 5 im Schrifttum mitgeteilten Fällen verglichen, wo genau gleichartige Veränderungen in den Lungen beschrieben worden sind, und in zwei von diesen kam gleichzeitig tuberöse Sklerose vor.

RÉSUMÉ

L'auteur relate un cas qui se caractériza cliniquement par une insuffisance respiratoire progressive au cours de bon nombre d'années. L'examen aux Rayons montra une augmentation généralisée du tissu interstitiel du poumon, et l'autopsie révéla, correspondant à l'image radiologique, une myomatose diffuse de ce tissu et des ganglions lymphatiques hilaires et médiastinaux, ainsi qu'une dilatation kystique généralisée des alvéoles et des bronchioles. Le cas est comparé à 5 autres rapportés dans la littérature, où précisément des altèrations semblables étaient décrites dans les poumons, et dans deux desquels il y avait en même temps de la sclérose tubéreuse.

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FROM THE RADIUM CENTRE, COPENHAGEN (CHIEF: JENS NIELSEN, M. D.)

BIOPSY WITH ROTATING TREPHINE FOR THE PURPOSE OF HISTOLOGIC DIAGNOSIS[1]

by

Harald Christiansen, M. D.

The histologic diagnosis is the keystone to the clinical structure which we seek to obtain in order to be satisfied with our diagnostical work; and perhaps especially in dealing with cancer it is of value to get this diagnosis established in order to enable us to institute a warrantable treatment and make it possible for us to form a judgement of the case on the basis of that treatment.

At the Radium Centre in Copenhagen we received, in 1940, 1074 new patients with malignant diseases. On 1044 of these, biopsy was made before treatment was instituted; that is to say that in 30 (= 3.5 per cent) there was no biopsy. In 18 of these we got histologic specimens by necropsy. Of our entire material there are thus 12 cases in which histologic diagnosis is lacking. Only in 8 cases was there disagreement between the histologic and the clinical diagnoses owing to mishaps about securing the specimens, and for one reason or another no second attempt was made.

A large number of the biopsies were made with conchotome or knife. Aspiration biopsy by means of a coarse cannula on a record syringe has gradually become limited to a small field; namely the rare cases in which we make liver-, spleen- and lung punctures and have been unable to obtain a biopsy in any other way. On the other hand, the use of a sharp, rotating trephine to secure the specimens has been used very extensively. In the 18 months since we began with this method, we have used it in 1527 cases of the most diverse affections, and of actual accidents we have only had two. In one case, in boring for the inguinal glands the trephine entered the femoral artery, but the bleeding was easily stopped by compression; in the second case I bored into the vesica in

[1] Read, with demonstration of films, at the meeting of the Northern Congress of Medical Radiology in Stockholm, June, 1941; submitted for publication Sept. 30, 1941.

trying to cut into the prostate through the perineum; but, as in the other case, without any resulting complications.

We have not observed any aggravation of the growth of the tumors, or any acute metastasising, as result of the biopsies. As regards melanomas we have been somewhat reserved, though. It never takes more than twenty-four hours, however, before we have the histologic diagnosis of the biopsy, and we attach some importance to this rapid service with the resulting early institution of the therapy; so that we have no hesitation about using the biopsy from fear of possibly furthering the development of metastases.

The technic of the operation will be understood from the film which I am going to show in a moment. I call attention especially to the strong suction with the record syringe in whitdrawing the trephine, the object of which is partly to tear the tissue column loose from its base, partly to keep it in place in the cannula.

We have used this method for obtaining tissue specimens from lymph-node tumors, and since we got the trephine we have not made a single extirpation of glands for the purpose of diagnosis. Surgical extirpation is a bigger affair, and as it leaves a cicatrix it cannot be repeated at will. There can be no objection to the trephining on these grounds, and as the tissue column obtained is quite large enough and its natural coherence has not been disturbed the histologist is satisfied with the result.

A large proportion of the trephine biopsies have been biopsies of the mamma. All our mammary tumors have been diagnosed histologically before pre-operative roentgen treatment was instituted, and our material enables us to compare the histologic specimens obtained before the treatment with those obtained after its conclusion and with the specimen from the operation. In our extensive use of trephine biopsies of the mamma we have several times met with surprises either in finding that some mammary affection of which we, clinically, were sure that it was malignant proved to be benign, for instance a plasmacellular mastitis or a deepseated abscess — or in discovering that an apparently benign affection was, in fact, malignant.

Biopsy of the prostate has in recent years been recommended especially by American authors, and the method used has been aspiration biopsy. The few times I have tried it I have not succeeded in getting any tissue out, and I therefore went over to using trephine biopsy instead. I let the cannula that has been used for the local anesthetisation, and which has been introduced perineally into the hard prostate under guidance of a finger in the rectum, remain in place as guide to the direction, cut its head off and then insert the trephine along the cannula. When the suction is applied both the column of tissue and the cannula come out.

1. 2.

Fig. 1. The cannula introduced into the body of a vertebra.

Fig. 2. The Trephine introduced into the vertebral body with the cannula serving as guide to the direction.

Roentgenologic diagnosis of pathologic processes in bones is uncertain. It can be difficult to decide from the roentgenologic image whether a »hole» in a bone is a metastasis, some kind of osteosarcoma, a melanoma or a giant-cell tumor. Besides, the defect in the bone often produces only local symptoms, so that the roentgenologic diagnosis does not get any support from the clinical observations. This is often the case with metastases from hypernephromas. In such affections we have in very short time and very easily obtained the diagnosis by trephine biopsy, and have thus been spared hopeless discussions and the waste of both time and money on examinations.

Trephine biopsy of the long tubular bones and of the bones of the pelvis presents no difficulties. In the case of osteosclerotic processes it is necessary to bore right through the bone and into the marrow cavity in order to obtain a column of tissue. For this purpose it is best to use a trephine with »drilling-crown». In biopsies of the spine — to obtain specimens from the bodies of the vertebrae — we have thought that a little more laborious method was better, and our technic has been to introduce a long, thin cannula obliquely until it was fixed in the body of the vertebra, the fixation being controlled by roentgen examination (Fig. 1); whereupon I have used this cannula as guide for the trephine,

just as in biopsy of the prostate (Fig. 2). I have used this method four times without complications, and have every time obtained pathologic tissue corresponding to the clinical picture.

SUMMARY

The author stresses the clinical importance of histologic diagnosis and describes the technic of making biopsies, with special mention of the method by which the tissue for examination is obtained by the use of a rotating trephine.

ZUSAMMENFASSUNG

Verf. hebt die klinische Bedeutung der histologischen Diagnose hervor, beschreibt die Technik der Biopsie und erwähnt besonders die Methode, nach welcher das zu untersuchende Gewebe mittels einer rotierenden Trephine entfernt wird.

RÉSUMÉ

L'auteur fait ressortir l'importance clinique du diagnostic histologique et décrit la technique des biopsies, en mentionnant spécialement la méthode du prélèvement à la tréphine tournante.

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MITTEILUNG AUS DER RÖNTGENABTEILUNG DES AMTSKRANKENHAUSES GENTOFTE
(LEITER: CHEFARZT ERIK DE FINE LICHT)

ÜBER LUNGENZYSTEN, BRONCHIEKTASEN UND LUNGENFIBROSEN, INSBESONDERE TUBERÖSE SKLEROSE[1]

von

Erik de Fine Licht

Die letzten Jahre haben eine umfangreiche Literatur über Lungenzysten und Bronchiektasen hervorgebracht, und einige in der letzten Zeit beobachtete Fälle haben es interessant erscheinen lassen, diese Leiden mit den Lungenfibrosen zusammenzustellen.

Bei den Lungenzysten sind es besonders die kongenitalen Formen, die in den Vordergrund treten. Abgesehen von den Echinokokkuszysten, die in gewissen Ländern und Gegenden eine grosse praktische Bedeutung haben, sind die erworbenen Zysten so selten, dass ich hier nicht näher auf sie einzugehen brauche, sondern nur erwähnen will, dass es sich besonders um Dermoidzysten handelt. Die Dermoidzysten enthalten oft Zähne und lassen sich in diesem Falle von den angeborenen geschlos. senen Zysten getrennt halten. Die Echinokokkuszysten können mit Hilfe der Komplementbindungsreaktion diagnostiziert werden.

Die angeborenen Zysten gehen augenblicklich unter einer Einheitsbezeichnung, nämlich als kongenitales zystisches Lungenleiden, welche Bezeichnung eine Reihe von Synonymen deckt, wie z. B.: fötale Bronchiektasen, angeborene Bronchiektasen, atelektatische Bronchiektasen, angeborene pulmonale Lymphangiektasie, offene Wabenlunge, Bronchiectasis universalis cystica und polycystic lungs. Möglicherweise gibt es noch mehr Namen, doch glaube ich, die am häufigsten angewandten aufgeführt zu haben. In der Literatur waren bis 1925 108 Fälle beschrieben, die von KOONTZ zusammengestellt wurden. 1937 vermochte SCHENCK insgesamt 374 Fälle zu sammeln. Hierzulande hat FLEMMING MØLLER als der erste, der in Skandinavien Zystenleiden in den Lungen röntgen-

[1] Vortrag, gehalten in der Dänischen Radiologischen Gesellschaft am 25. 10. 41; bei der Red. am 15 Jan. 1942 eingegangen.

diagnostizierte, die Liste mit 6 eigenen Fällen ergänzt, von denen der eine sogar mit ausgezeichnetem Erfolg von P. N. HANSEN operiert worden war.

SCHENCK schliesst sich ANSPACH & WOLMAN an, indem er die Zysten in solitäre Zysten mit oder ohne Verbindung zu den Bronchien und in multiple Zysten mit oder ohne Verbindung zu den Bronchien einteilt. Bei den Zysten, die eine Verbindung haben, unterscheidet er zwischen solchen, welche eine freie Verbindung haben, und denen, die eine Ventilverbindung haben. Mittels dieser Einteilung gelingt es ihm, nachfolgendes Schema 1 aufzustellen.

Schema 1.

ANSPACH & WOLMAN's *Schema* (*modifiziert*).

A. Solitärzysten (bei der Geburt mit Flüssigkeit gefüllt).
   1. Ohne Kommunikation mit Bronchien — — — — Solitäre flüssigkeitsgefüllte Zysten.
   2. Mit Kommunikation mit Bronchien — — — — Solitäre Luftzysten.
      a. Freie Öffnung — — — nicht ausdehnbare Luftzysten.
      b. Ventilöffnung — — — ausdehnbare Luftzysten.

B. Multiple Zysten (bei der Geburt mit Flüssigkeit gefüllt).
   1. Ohne Kommunikation mit Bronchien — — — — Multiple flüssigkeitsgefüllte Zysten.
   2. Mit Kommunikation mit Bronchien — — — — Multiple Luftzysten.
      a. Freie Öffnung — — — nicht ausdehnbare Luftzysten.
      b. Ventilöffnung — — — ausdehnbare Luftzysten.

Das kongenitale Zystenleiden ist eine Entwicklungsmissbildung, die einen beliebigen Teil des Bronchialbaumes oder das interstitielle Lungengewebe angreifen kann. Das Leiden kann Teile der Lunge oder die ganze Lunge umfassen, was sowohl von der multiplen als auch von der solitären Form gilt. Der Zysteninhalt besteht bei der Geburt aus einer milchigen oder unklaren Flüssigkeit, und die Zysten können gefüllt bleiben oder sie können auch bersten und so Luftzysten bilden. Wenn die Verbindung zu den Bronchien nach dem Zerplatzen offen und frei ist, ist die Zyste stationär; ist die Verbindung ventilartig, so wird die Zyste expansiv, was sowohl für die solitären als auch für die multiplen Zysten gilt. Unter den 374 von SCHENCK besprochenen Zystenfällen gab es 141 solitäre Zysten und 233 multiple. Die rechte Lunge hatte 42 %, die linke Lunge 37 %, und in 21 % waren die Zysten doppelseitig. In Schema 2 sieht man die Verteilung der verschiedenen Typen bei Erwachsenen und bei Kindern.

Schema 2.

Verteilung der Zysten nach SCHENCK.

Solitärzysten.	Kinder	Erwachsene	Insgesamt
Flüssigkeitsgefüllte Zysten	28	21	49
Nicht ausdehnbare Luftzysten	22	33	55
Ausdehnbare Luftzysten	32	5	37
Insgesamt Solitärzysten	82	59	141
Multiple Zysten.			
Flüssigkeitsgefüllte Zysten	25	13	38
Nicht ausdehnbare Luftzysten	50	138	188
Ausdehnbare Luftzysten	5	2	7
Insgesamt	80	153	233

Die Pathogenese ist unbekannt. Es wird angenommen, dass eine kleine Lungenknospe abgeschnürt und zu Lungengewebe weiterentwickelt wird, sowie dass das abgesonderte Sekret die Wände nach aussen presst. Nach LIESE entstehen die Solitärzysten, wenn die Missbildung zu einem frühen Zeitpunkte der durch dichotonische Teilung vor sich gehenden Entwicklung des Bronchialbaumes eintritt; die multiplen Zysten dagegen entständen, wenn die Missbildung später in der Entwicklung vor sich gehe, während die Teilung bereits ziemlich weit vorgeschritten sei. Sehr oft finden sich, wie schon von FLEMMING MØLLER 1928 hervorgehoben wurde, die Zysten in atelektatischen Lungenlappen, besonders in akzessorischen Lappen.

Die Symptome sind je nach der Lokalisierung, Art und Grösse der Zysten variierend. Dyspnoe und Zyanose kommen meist bei ausdehnbaren Zysten vor und verschwinden erst, wenn die Zysten punktiert werden oder die Luft in anderer Weise aus ihnen entweichen kann, z. B. durch Zerplatzen zur Pleura hin oder durch Wegoperieren der Zyste. Die Expektoration hängt davon ab, ob eine Verbindung zu den Bronchien besteht und ob Infektion eintritt; in diesem Falle kann das Krankheitsbild ganz dem ähneln, welches man bei erworbenen Bronchiektasen findet. Hämoptyse ist nicht selten, und Schmerzen können vorkommen.

Die Diagnose der angeborenen Lungenzysten beruht hauptsächlich auf der Röntgenuntersuchung, und nicht selten findet man durch die Röntgenuntersuchung Zystenleiden bei einem Patienten, der im grossen und ganzen keine nennenswerten Symptome zeigt. Das gilt besonders von der Gruppe, die an der als offene Wabenlunge bezeichneten Form leidet. Für das Röntgenbild charakteristisch ist, dass die Veränderungen sich lange Zeit hindurch bei verschiedenen Untersuchungen unverändert halten.

Die gefüllten Solitärzysten geben einen recht intensiven Schatten, etwas schwächer als der Herzschatten und rundlich. Die Differentialdiagnose

steht zwischen Tumor und anderen Zystenformen. Man muss sowohl an maligne als auch an benigne Tumoren denken, und von den letzteren kommen Chondrome und die fast stets linksseitigen Ganglionneurome in Betracht. Die Tumoren dürften oft stärker schattengebend und schärfer begrenzt sein, als Zysten zu sein pflegen. Echinokokken und Dermoide habe ich bereits erwähnt. Pneumonische Infiltrate, abgekapselte Exsudate, Empyeme und Lungenabszesse können ein ähnliches Bild wie Zysten geben, doch wird hier in den meisten Fällen die Klinik zu der richtigen Diagnose verhelfen. Mitunter ist Punktion der Zyste möglich, wobei der Inhalt von milchiger Flüssigkeit zur Diagnose beitragen kann. Injiziert man Abrodil, so vermag man bei Zystenbildungen mitunter den Kontrast in den Lymphbahnen der Umgebung einige Stunden später zu sehen.

Solitäre nicht ausdehnbare Luftzysten stellen einen kugelförmigen oder sphärischen Luftraum dar. Oft kann man eine dünne Kapsel um denselben unterscheiden. Differentialdiagnostisch kommen hier gewisse Fälle von bullösem Emphysem in Betracht (JACOBAEUS), sowie lokaler Pneumothorax. Hierbei ist im Gegensatz zur Zyste keine Kapsel vorhanden, und Pneumothorax ist selten so regelmässig. Kavernen und Abszesse dürften anamnestisch meistens anders verlaufen.

Eine solitäre ausdehnbare Zyste mit zunehmender Dyspnoe kann einem totalen Pneumothorax ähneln. Das Zwerchfell ist abgeflacht, und der Mediastinalschatten wandert zur gesunden Seite hin. Diaphragmawinkel und Apex sind oft verschattet, weil das Lungengewebe in diese Regionen hinausgedrängt und atelektatisch wird. Der übliche Schatten der komprimierten Lunge fehlt im Hilus. Wird ein Pneumothorax angelegt, so kann man die Zyste auf dem Röntgenbilde zum Erscheinen bringen. Mitunter vermag man sie ohne Anlegung eines Pheumothorax zu sehen.

Multiple Luftzysten werden durch ihre scharfgezeichneten sphärischen Kavitäten und das Fehlen einer Infiltration zwischen denselben charakterisiert. Mitunter sieht man Trabekeln und hin und wieder Flüssigkeitsspiegel. Wenn es nicht zu Infektion gekommen ist, fehlen klinische Symptome, was dazu dient, diese Zysten von erworbenen Bronchiektasen zu trennen.

Gewöhnliches bullöses Emphysem, welches röntgenologisch sehr ähnlich ist, sitzt meistens basal; doch kann die Differentialdiagnose schwierig sein.

Bei Bronchiektasen sind in der Regel viele sekundäre Veränderungen vorhanden; aber in gewissen Fällen kann man keine Differentialdiagnose stellen, und viele Autoren sind der Ansicht, dass man von der Stellung einer Differentialdiagnose absehen müsse, sobald sekundäre Veränderungen in den Zystenfällen vorkommen.

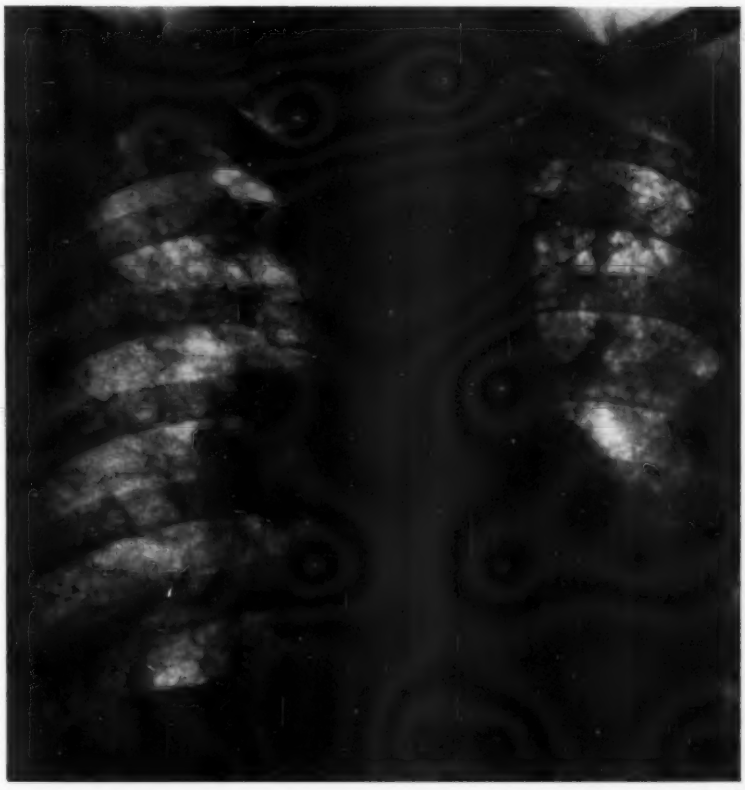

Fig. 1. Gewöhnliche Röntgenaufnahme unserer Patientin mit tuberöser Sklerose. Die interstitiellen Veränderungen sind besonders deutlich. Keine sicheren Zystenbildungen.

Bronchographie kann zuweilen zur Diagnose verhelfen, da Bronchiektasen in der Regel gefüllt werden, und das gleiche gilt von leichteren Formen von bullösem Emphysem (JÄDERHOLM); zwischen den Zysten werden dagegen oft Hohlräume sein, wo die Verbindung mit den Bronchien so fein ist, dass der Kontraststoff nicht eindringt. Von entscheidender Bedeutung ist dieses Verhalten jedoch nicht. Bei den solitären Zysten gibt es oft Missbildungen von selbst sehr grossen Bronchien, sodass sie deutlich blind enden.

Die Prognose des Zystenleidens hängt von der Anzahl, der Grösse, dem Typus und der Lokalisation, von dem Alter des Patienten sowie davon ab, ob Infektion vorhanden ist. Obschon der Zustand nicht unver-

Fig. 2. Tomographische Aufnahme der l. Lunge unserer Pat. mit tuberöser Sklerose. Man sieht nach oben zu mehrere zystische Hohlräume.

Fig. 3. Gewöhnliche Röntgenaufnahme der l. Lunge unserer Pat. mit tuberöser Sklerose, nachdem die Lunge bei der Autopsie herausgenommen worden ist. Man sieht deutlich nach oben zu die grossen Zysten und nach unten zu die zahlreichen Hohlräume von weit geringerem Umfange.

einbar mit einer langen Lebensdauer ist, ist doch die Mortalität hoch, namentlich bei Kindern, und zwar insbesondere bei den ausdehnbaren Zysten. Die chirurgische Therapie ist die einzige rationelle, wenn die Möglichkeit zu ihrer Ausführung besteht. SAUERBRUCH hat bei 58 Lobektomien aufgrund angeborener Zysten 6 Todesfälle und 51 vollkommene Heilungen ohne Fistelbildung. Die Operation soll relativ frühzeitig ausgeführt werden, ehe Infektion eintritt. Spontanheilung infolge von Zerplatzen und darauf dauerndem Zusammenfallen der Zyste hat SCHENCK nur in 5 der gesammelten 368 Fälle gefunden, sodass diese Chance also gering ist.

Wenn man die Zystenliteratur durchsieht, stösst man auf einige verstreute Fälle, die nicht richtig in das bisher geschilderte Bild hineinpassen und die man auch nicht beschrieben findet, wenn man die Berichte über die erworbenen Bronchiektasen studiert. Dr. ROSENDAL zeigte im vorigen Jahre einen solchen Fall in der Radiologischen Gesellschaft, und ich habe selbst kurz darauf Gelegenheit gehabt, einen derartigen Fall bei der Sektion zu sehen, nachdem die Patientin ein Jahr vorher von mir röntgenuntersucht worden war.

Mein Fall war eine 63jährige, verheiratete Frau, die auf die medizinische Abteilung F des Kopenhagener Amtskrankenhauses Gentofte am 1. 12. 1939 aufgenommen wurde. Sie war bis zum Beginn des jetzigen Leidens gesund gewesen. Sie hatte einmal geboren; die Tochter bekam Epilepsie und befindet sich jetzt in dem Nervensanatorium Philadelphia. Ein Jahr vor ihrer Aufnahme hatte die Patientin begonnen, an Atemnot zu leiden, und konnte nur mit Mühe Treppen steigen. $^3/_4$ Jahre lang hatte sie »Bronchitis» ohne Fieber, aber mit Husten und Expektorat, gehabt. In den letzten Monaten vor ihrer Krankenhausaufnahme waren Schmerzanfälle in der linken Thoraxhälfte bis in den linken Arm hinaus aufgetreten; die Schmerzen verschwanden bei Ruhe. Grössere Mahlzeiten genügten, um der Patientin Dyspnoe zu geben, weswegen sie nur wenig ass. Bei der objektiven Untersuchung fand man ein dem Alter entsprechendes Aussehen. Es existierte eine leichte Ruhedyspnoe, leichte Zyanose der Lippen, nichts Abnormes im Rachen, aussen am Halse oder an der Schilddrüse. Steth. cordis: Grenzen Costa 4 und linker Sternalrand. Herzstoss ein wenig ausserhalb der Medioklavikularlinie. Töne dumpf. 2. Pulmonalton akzentuiert. Aktion regelmässig, etwas schnell. — Steth. pulm: Über der ganzen Rückenfläche mittelfeine Rassellaute und einzelne Ronchi. Abdomen natürlich. Hepar bis zur Kurvatur. Extremitäten natürlich. Keine Oedeme.

Pat. wurde auf der Abt. F bis zum 18. 1. 40. behandelt. Expektoratuntersuchung zeigte keine Tb., weder im Expektorat noch im Spülwasser. Mantoux —. Hämogl. war 94. Blutdruck 140/70. S. R. 63. WaR. negativ. Gewicht 53, 8. 8 Monate nach der Entlassung wurde sie auf die Abt. B aufgenommen. Die Anfälle waren nun beträchtlich verschlimmert. Die Schmerzen waren konstant geworden, und ein besonders heftiger Schmerzanfall in der vorausgehenden Nacht war der Grund der Einlieferung. Pat. hatte seit ihrem Aufenthalt auf Abt. F wegen ihrer Dyspnoe im Rollstuhl gefahren werden müssen. Sie hatte noch immer trockenen Husten, doch jetzt ohne Auswurf. Steth. und objektive Untersuchung ergab ausser starker Zyanose keine Veränderungen gegenüber früher. Es ging ihr eine Zeitlang einigermassen; aber am 9.10. verfiel sie stark und starb am 10.10.41.

Während des Aufenthaltes auf der Abt. F wurde die Pat. röntgenuntersucht (Fig. 1—2), wobei sich folgender Befund ergab: 5/1239. Beide Lungenfelder zeigten beträchtliche Veränderungen, die auf der l. Seite am stärksten ausgeprägt waren. Man sieht eine starke, netzartige Zeichnung, die aus zahlreichen feinen Strichen und unregelmässigen Schattenflecken besteht, und zwischen diesen Veränderungen finden sich rundliche Aufhellungen angedeutet. Die Kontur des Herzens ist auf der l. Seite fast ganz verwischt, und gleichzeitig besteht eine leichte Retraktion nach links. Am 6. 12. 39 wurde Tomographie mit der Pat. in Rückenlage und mit Schnitt 10 cm über dem Tisch vorgenommen. Hierbei sieht man auf der l. Seite zahlreiche Aufhellungen von 10 Øre-Grösse und mit recht dichten Rändern. Der r. Hilus ist besonders kräftig. Es liegt anscheinend eine Bronchiolitis in Verbindung mit einem interstitiellen Prozess vor. Über die Ursache lässt sich nichts Sicheres aussagen. Die zahlreichen Aufhellungen wecken Verdacht auf Tuberkulose, aber möglicherweise handelt es sich um Bronchiektasen. Man muss ausserdem an die Möglichkeit von Boecks Sarkoid, Syphilis, sowie Lungenbilharziose denken.

Fälle von reiner Bronchiolitis mit Bronchiektasen kommen vor, ohne dass man die Ursache hat nachweisen können. Einer Pneumokoniose, Miliartuberkulose, Stase und Karzinose gleicht das Bild nicht richtig. Diagnose Bronchiolitis mit Bronchiektasen? Tub. pulm. fibro-cavernosa. Da nichts Klinisches auf Tuberkulose hindeutete, wurde die Diagnose: Bronchiolitis mit Bronchiektasen.

Die Sektion (Prosektor VINTRUP) zeigte Bronchiektasia cavernosa universalis pulm. Induratio pulm. Thrombosis parietalis aortae et auriculae d. cordis. Arteriosclerosis. Hypertrophia ventriculi d. cordis.

Der l. oberste Lungenlappen (Fig. 3) zeigt zahlreiche erbsen- bis knapp haselnussgrosse Zysten, die auf der Oberfläche hervorragen, während die Lunge im übrigen braun und grob gekörnt ist mit abgeflachten Granula von ca. halber Erbsengrösse, welche ganz dicht liegen. Das Gewebe fühlt sich fest an, und es gibt kein Luftknittern. Auf dem Schnitt sieht man im l. obersten Lappen, dass die erwähnten Zysten bronchiektatische Kavernen mit glatter Wand vorstellen; sie sind sehr zahlreich und liegen ganz dicht aneinander, durch gräuliches Bindegewebe mit Gefässen getrennt. Im untersten Lappen finden sich ungeheuer zahlreiche gerade noch sichtbare oder ca. 2 mm grosse Bronchiektasien überall vor, auch ganz aussen in den granulären Vorsprüngen unter der Pleura. Die Bronchien zeigen charakteristischen Knorpelschwund und sackförmige Ektasien mit dazwischenliegenden Schleimhautvorsprüngen. Die r. Lunge ist etwas grösser als die l. und zeigt im grossen und ganzen das gleiche Bild wie der l. unterste Lappen, ist jedoch in höherem Grade induriert, und es ist schwierig, Gewebe zu finden, das auf Wasser schwimmen kann. Es finden sich keine pneumonischen Prozesse vor, und in den Bronchien ist nur sehr spärlicher Schleim vorhanden. Keine Tuberkulose. R. Pleura ist natürlich, auf der l. sind fibrilläre Verwachsungen. Hepar hat nat. Grösse; es gibt eine charakteristische kardiale Zirrhose mit Muskatnusszeichnung. Cor zeigt die r. Herzhälfte hypertrophisch. R. Auricula ist thrombosiert. Kein Klappenleiden. Das Myokard ist braun und zäh. In der Aorta findet sich eine heftige Atheromatose und Sklerose mit Verkalkung und parietaler Thrombose, teils in der Pars thoracalis, teils gerade gegenüber der Bifurcatio aortae.

Histologische Untersuchung der Lungen

Im Schnitt von der r. Lunge findet sich erhebliche Induration des Gewebes. Grösstenteils gibt es reichliches Bindegewebe zwischen den Alveolen, und breite Züge von gefässreichem Gewebe fibröser Natur kommen entlang den dünnwandigen Arterien vor. Die Bronchialäste sind im Verhältnis zu den Dimensionen der Lunge dünnwandig. Man sieht nur spärlichen Knorpel. Die Muskulatur ist in einigen Bronchialästen relativ kräftig und tritt in der Form isoliert gelegener zirkulärer Bündel mit dazwischenliegendem, entzündungsinfiltriertem, fibroplastischem Gewebe auf. Die Schleimhaut ist sehr dünn, bekleidet mit abgeflachtem Epithel. In einigen Bronchialästen kommt jedoch Zylinderepithel vor. Andere Äste enthalten Eiter mit grossen, konzentrisch geschichteten Körpern, Corpora amylacea, wie man es z. B. bei der chronischen suppurativen Galaktophotritis des Rindes findet. In Stücken von der l. Lunge nahe des Hilus zeigt sich eine enorm kräftige Muskulatur in der Bronchialwand. Die Schleimhaut wird nach dem Lumen zu von einer sehr ins Auge fallenden Membrana propria, die sich stark mit Säurefuchsin färbt, abgeschlossen, worauf eine Schicht ganz abgeflachter Zellen folgt, welche hauptsächlich an ihren Kernen zu erkennen sind. Es gibt recht guterhaltene Drüsen ausserhalb der Muskularis, die Knorpelringe sind bewahrt. Die kleineren Bronchialäste bieten das gleiche Bild wie in der r. Lunge. Das Lungengewebe selbst ist hyperämisch und induriert, freilich nicht in so hohem Grade wie in der r. Lunge. Die mikroskopische Diagnose lautet auf Bronchiektasiae. Bronchitis chron. suppurativa. Induratio pulm.

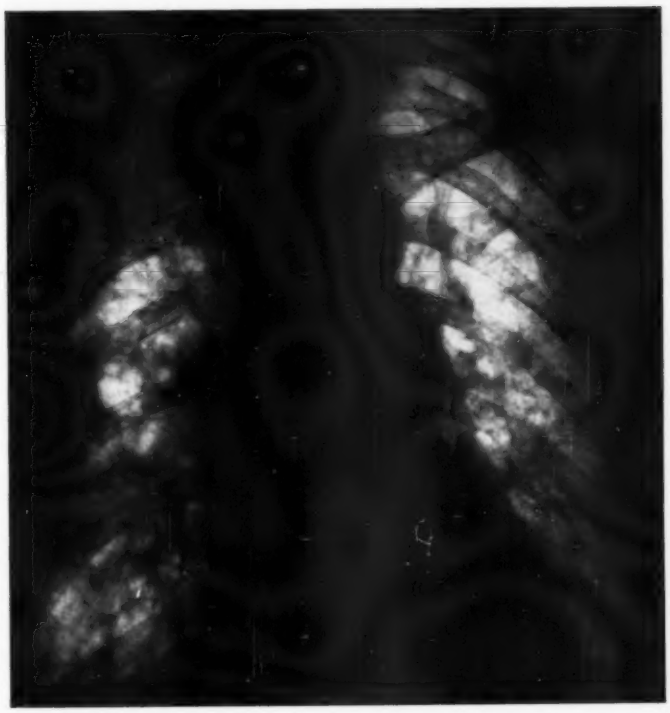

Fig. 4. Doppelseitige Wabenlunge mit Pneumonie in r. Lunge. Durch die Autopsie verifiziert. Keine interstitiellen Veränderungen chronischer Art.

Weder klinisch noch röntgenologisch ähnelt dieser Fall dem oben geschilderten angeborenen Zystenleiden der Lungen (Fig. 4). Klinisch sieht man eine auffallende Progredienz von Gesundheit zu Tod im Verlaufe von nur 2 Jahren. Das geschieht, ohne dass irgendeine eigentliche Infektionskrankheit zur Stelle ist, ohne Fieberanfall und mit zunehmender Dyspnoe, Schmerzen sowie etwas Husten mit Expektorat als einzigen Symptomen.

Röntgenologisch zeigt die gewöhnliche Aufnahme eine ausgebreitete Fibrose in beiden Lungen ohne sichere Hohlräume. Erst bei der tomographischen Untersuchung gelingt es, dieselben mit einer recht grossen Sicherheit festzustellen, und man kann eine Wahrscheinlichkeitsdiagnose auf Bronchiectasia cystica stellen, da die Klinik gegen Tuberkulose spricht. Ohne Tomographie würde das Bild in eine Klasse mit den Lungenfibrosen kommen, wie man sie bei Silikose, speziell bei der Asbestose, sieht, welche

nach einigen Autoren besondere Neigung zur Bildung überwiegend interstitieller Veränderungen zeigen soll, sowie schliesslich bei Syphilis. Fernerhin können gewisse nichtfibröse Leiden ein ähnliches Bild geben, wie Boecks Sarkoid, Miliartuberkulose (bei welchem Leiden namentlich die ausgeheilten Fälle Schwierigkeiten bereiten könnten), Karzinose, Bronchiolitis nach Influenza, gewisse Formen von Leukämie und Lymphogranulomatose und schliesslich gewisse Speicherkrankheiten sowie Lungenbilharziose.

Den üblichen Formen erworbener Bronchiektasen gleicht das Bild nicht. Sie sind nicht so ausgebreitet und geben klinisch ganz andere Symptome; aber abgesehen davon, kann man wohl sagen, dass eine gewisse Ähnlichkeit im Röntgenbilde existiert. Pathologisch-anatomisch gilt etwas Ähnliches, die Ausbreitung ist zu gross und die Entzündung zu gering; aber sonst gleicht das Bild in Einzelheiten.

Ich habe in der Literatur 3 Fälle gefunden (KERLEY, SHORE and YOUNG, NOLTE, WEISS), die in jeder Weise meinem eigenen Falle gleichen, sowohl klinisch, röntgenologisch als auch makroskopisch bei der Sektion. Die Diagnose war freilich in keinem von ihnen vorher gestellt worden. Die Fälle sind alle als vermutlich erworbene Zystenbildungen veröffentlicht worden, aber es ist kaum in einem der Fälle möglich, das mit Sicherheit festzustellen. Die Probleme, welche sich melden, wenn man solchen Fällen gegenübersteht, bestehen in erster Linie in der Frage, was das Primäre ist. Sind es angeborene Veränderungen, die aus einem oder dem anderen Grunde Anlass zu einem heftigen interstitiellen Prozess geben, oder ist es umgekehrt ein interstitieller Prozess, der das Primäre ist und dann sekundäre Bronchiektasien hervorruft, oder liegt eine Mischung von beiden vor oder eine zystische Degeneration in einem Tumor? Die Lösung dieser Probleme muss den Pathologen überlassen bleiben.

Abgesehen von diesen Fragen, bilden diese Leiden eine interessante Gruppe, und kürzlich veröffentlichte Fälle aus Schweden werfen ein ganz neues Licht auf solche Zustände. Die betreffenden Fälle umfassen 3 Geschwister. Bei 2 von ihnen, 2 Schwestern, liegt das gleiche Lungenbild wie in unserem Falle vor. Die eine ist gestorben, und bei der Sektion fand man, dass ein Fall von tuberöser Sklerose vorlag, welche vorher nicht in den Lungen nachgewiesen worden war. Die pathologisch-anatomische Untersuchung stammt von VEJLENS, der nachwies, um BERG & ZACHRISSON's Beschreibung des Falles in den Acta radiologica zu zitieren, dass das Lungenbild »an und für sich selbst einzigartig war, doch dass es nur ein Glied in einem ausgedehnten endogenen Systemleiden, nämlich der tuberösen Sklerose, darstellte». Bei der Sektion wurden nachgewiesen Pringles Naevi im Gesicht, subunguale Fibrome an den Nägeln, Veränderungen in den eosinophilen Zellen der Hypophyse,

Atrophie in den Ovarien, tuberöse Veränderungen im Gehirn, tuberöse Veränderungen in den Nieren, tuberöse Veränderungen in einer Lymphdrüse und schliesslich ein Splenom. Bei der noch lebenden Schwester wurde, wie erwähnt, ein ganz gleiches Lungenbild gefunden, und während man in dem ersten Falle die Diagnose Induratio pulm. gestellt hatte, konnte man nun die Diagnose Bronchiektasen und Induratio pulm. stellen. Diese Schwester hatte ausserdem Fibroma subunguale und Pringles Naevi, sie war etwas dyspnoeisch und hält nicht recht viel Arbeit aus. Sie hatte weiterhin einen Tumor in der hinderen Scheidenwand gehabt, der entfernt wurde und sich als ein Myom von embryonalem Charakter erwies (VEJLENS). Ein Bruder hatte Adenoma sebaceum und suprazelluläre Verkalkungen im Gehirn. Die übrigen Familienangehörigen waren gesund.

Die tuberöse Sklerose wird in der Literatur um 1920 herum ziemlich viel besprochen. Sie wird auch Bournevilles Krankheit genannt nach der Beschreibung, die derselbe 1880 von ihr gegeben hat. Klinisch sind ihre Hauptsymptome in ihren ausgeprägten Formen: Geistesschwäche, Krämpfe und Pringles Naevi oder Adenoma sebaceum in der Haut, besonders im Gesicht. Sind diese Symptome vorhanden, so ist die Diagnose nach KRABBE sicher. Das Leiden tritt häufig familiär auf. Man war sich bald klar darüber, dass das Leiden mit weniger ausgesprochenen Gehirnsymptomen auftreten konnte, sowie dass es sich um eine Systemerkrankung handelte. Es lassen sich eigentümliche tumorartige Veränderungen im Herzen, in den Nieren und in den Lymphdrüsen nachweisen, wie z. B. Leiomyome oder lipomatöse Veränderungen in den Nieren und Rhabdomyome im Herzen, und diese Zustände können in gewissen Fällen das Krankheitsbild beherrschen. Die Rhabdomyome führen schnell zum Tode. Das Nierenleiden kann sogar einer Sarkomatose mit malignem Wachstum und Metastasierung ähneln (KIRPICZNICK). KRABBE nennt das Leiden eine Phakomatose, und es ist an und für sich nicht merkwürdig, dass es in den Lungen auftritt; doch ist es bisher in der Literatur nicht an diesem Organ lokalisiert worden.

Die Frage war für uns, ob man in unserem Falle nun nachträglich das Leiden als eine tuberöse Sklerose diagnostizieren konnte, trotzdem das Gehirn nicht untersucht worden und im Krankenjournal nichts über Adenoma sebaceum angeführt worden war. Ob die Lungenveränderungen an und für sich genügend charakteristisch sind, muss eine Frage bleiben, zu der die Pathologen Stellung zu nehmen haben. Ich wandte mich an »Philadelphia», wo sich die Tochter befand, um dieselbe bezüglich der Lungen röntgenuntersucht zu bekommen, und erhielt von Chefarzt Dr. med. STUBBE TEGLBJERG die Antwort, dass das aus apparatmässigen Gründen erst in einem Monat möglich sei; zugleich erhielt ich aber auch die wertvolle Mitteilung, dass die Tochter an tuberöser Sklerose leide.

Dieser Aufschluss bei einem so seltenen Leiden von familiärem Charakter macht es ja fast sicher, dass es sich bei unserer Patientin um einen Fall von tuberöser Sklerose mit dominierendem Lungenleiden gehandelt hat.

Einige Autoren haben Mb. Recklinghausen und tuberöse Sklerose in Verbindung miteinander gesetzt. MARCUS hat hier im Norden davon Abstand genommen. Es gibt indessen andre seltene Leiden, die ähnliche Lungenbilder bei der Röntgenuntersuchung geben können. Hand-Schüller-Christians Krankheit kann Lungenfibrose geben, und ich habe bei FREEMAN einen Fall von Xanthomatose gefunden, wo die Sektion ungefähr das gleiche makroskopische Bild zeigte wie bei den Patienten, mit denen wir uns hier beschäftigen. Es ist in diesem Zusammenhange von Interesse, dass BERG & ZACHRISSON's dritter Fall, der nicht mit den anderen erwähnten Personen verwandt war, an Diabetes insipidus leidet, welcher zusammen mit Exophthalmus und ossösen Schädelveränderungen typisch für Hand-Schüller-Christians Krankheit ist. Hiermit sei nicht gesagt, dass es sich um dieses Leiden handelt, welches man freilich bisher nicht ohne die Schädelveränderungen kennt. Es geht nicht aus dem Artikel hervor, ob der Schädel untersucht worden ist; da aber die Untersuchungen in allen Fällen anscheinend sehr gründlich gewesen sind, ist es sicher geschehen. Bei dem Pat. fehlen Pringles Naevi, und es muss vorläufig dahingestellt bleiben, was hier eigentlich vorliegt. Auch wir haben Fälle, die röntgenologisch ähneln, und in TESCHENDORFF's Buch werden gerade Fälle von Bronchiolitis besprochen, bei denen der Zustand sich lange Zeit hindurch ganz unverändert hält und wo man keinerlei klinische Diagnose stellen kann; in Zukunft müssten solche Fälle weiter verfolgt werden.

Anlässlich unseres und der anderen vorliegenden Fälle glaube ich feststellen zu können, dass innerhalb der Literatur über das angeborene zystische Lungenleiden Fälle veröffentlicht worden sind, die ausser durch das Zystenleiden durch universelle interstitielle Lungenveränderungen, welche das Bild beherrschen, charakterisiert werden, sodass die Zysten nur schwer zu sehen sind. Eine vorherige, dann durch die Sektion bestätigte Diagnose liegt nur in meinem Falle vor. Ein Teil dieser Fälle wird sich zweifellos als von tuberöser Sklerose verursacht erweisen; doch muss man vorsichtig damit sein, sie alle zu dieser Krankheit zu rechnen. Namentlich muss man auf seinem Posten sein mit Hinblick auf »Speicherungs»-krankheiten, insbesondere Hand-Schüller-Christians Krankheit. Möglicherweise werden auch andere Leiden dasselbe Bild geben können. Krankheiten dieser Art dürfen nicht mehr unter das angeborene zystische Lungenleiden gerechnet werden, da die Möglichkeit, dass es sich um interstitielle Veränderungen systematischen Charakters handelt, erheblich ist. Tomographische Untersuchung ist von grossem Wert bei solchen Röntgenbildern, und wenn die Dyspnoe beträchtlich ist, muss man sicher

auf eine Bronchographie verzichten, die sonst vielleicht von Nutzen sein könnte.

ZUSAMMENFASSUNG

Nach einer Übersicht über die neueren Gesichtspunkte betreffs der Einteilung der Lungenzysten und nach einer kurzen Besprechung der differentialdiagnostischen Verhältnisse, insbesondere gegenüber den Bronchiektasen, wird ein Fall von Lungenfibrose mit multiplen doppelseitigen Bronchiektasen mitgeteilt, der bei der Autopsie verifiziert wurde und wahrscheinlich im Gefolge einer tuberösen Sklerose entstanden war. Der Wert der tomographischen Untersuchung zur Unterscheidung dieses Falles von den eigentlichen Lungenfibrosen wird hervorgehoben. Eine Literaturdurchsicht scheint zu zeigen, dass mehrere ähnliche Fälle unter die Lungenzysten eingeordnet worden sind; man muss aber soweit wie möglich zukünftige Fälle ausserhalb des Begriffes Lungenzysten halten. Vermutlich werden eine Anzahl Fälle, ebensowie VEJLENS' und unser Fall, unter die tuberöse Sklerose fallen; doch scheint die Möglichkeit zu bestehen, dass auch andere Leiden ähnliche Zustände geben können.

SUMMARY

The author reviews the latest points of view according to which lung cysts have been grouped, discusses in brief the possibility of differential diagnosis, especially between bronchiectases, reports a case of fibrosis of the lungs with multiple bilateral bronchiectases, which were proved at autopsy and which most likely were sequels of tuberous sclerosis. The value of tomographic examination for differentiation between such conditions and a true case of fibrosis of the lungs is stressed. A study of the literature makes the author inclined to believe that several similar cases have been grouped among cases of lung cysts. It is, however, of importance that such cases are discriminated from lung cysts in the future. Most likely a number of cases, as well as VEJLENS' case and the case reported in this paper are sequels of tuberous sclerosis; the possibility, however, seems to exist, that also other affections may cause similar conditions.

RÉSUMÉ

L'auteur passe d'abord en revue les conceptions les plus récentes touchant le classement des kystes pulmonaires et traite brièvement des diagnostics différentiels, en particulier avec les bronchectasies, puis il relate un cas de fibrose pulmonaire accompagné de bronchectasies multiples bilatérales, qui fut vérifié à l'autopsie et était vraisemblablement consécutif à une sclérose tuberculeuse. Il souligne la valeur de l'examen tomographique pour distinguer ce cas des fibroses pulmonaires proprement dites. Une revue de la littérature paraît montrer que plusieurs cas semblables ont été rangés parmi les kystes des poumons; mais il faudra, autant que faire se pourra, exclure les cas à venir de l'entité des kystes pulmonaires. Il est à présumer qu'un certain nombre de cas, comme celui de VEJLENS et le nôtre, ressortiront à la sclérose tubéreuse; il paraît cependant possible que d'autres affections encore puissent créer des états analogues.

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BY ROENTGENOGRAPHY STATED REDUCTION OF THE CALCIFIED FOCUS IN PRIMARY PULMONARY TUBERCULOSIS IN CHILDHOOD[1]

by

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The opinions about the course of the calcified primary pulmonary focus in childhood are greatly varying. In his extensive studies on primary tuberculosis in childhood, based on findings in literature, WALLGREN discusses also this question in detail. His personal experience is »that the complex may undergo considerable regressive changes, though he did not have an opportunity of following a case so far as to be able to ascertain a complete disappearance of the calcified focus previously visible on the roentgen film». In the two cases which WALLGREN gives as examples the reduction in size of the calcified primary complex in the course of about ten years indeed is considerable. WALLGREN believes that the regression could progress so far that the calcium finally was totally replaced by connective tissue. BRAILEY concluded from her extensive roentgenologic studies on the development of intrathoracic calcification in tuberculin positive infants, that small deposits of calcium may become indistinguishable with time, due to changes in the calcified mass, or to its becoming hidden by mediastinal structures. She could cite only one instance of absorption and disappearance of a calcified parenchymal nodule in a young child within four years of its first appearance. In this case calcification of the corresponding tracheobronchial lymph nodes, first recorded after the calcified pulmonary nodule was seen, was still evident when no trace of the nodule could be found any more. In a recent roentgenological study the possibility of a total disappearence of the calcified focus was also mentioned by SWEANY.

With regard to this question of the disappearance of the calcified primary focus, the contrast between the results of the roentgenological

[1] Submitted for publication Aug. 3, 1941.

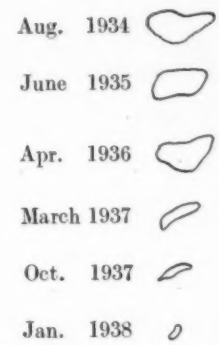
study during life and of postmortal studies always has to be considered. In this connection an earlier publication of SWEANY among others must be mentioned. He made use of a special method by which he was able to locate roentgenologically calcifications as small as a millimeter in diameter in lungs, obtained at autopsy. With this sensitive method definite calcifications were seen on postmortem radiographs twice as frequent as on the antemortem films. — From SWEANY's results thus may be concluded that a total disappearance of the calcified focus will rarely occur. The same conclusion can be drawn when BEITZKE's opinion is accepted; after this author total disappearance of the calcified focus cannot take place before the tubercle bacilli present in the focus are dead. A complete disappearance of the calcifications in all tuberculous foci thus would mean that the patient should lose his sensitivity to tuberculin. As this occurs rarely, a complete disappearance of the calcification will also occur seldom (WALLGREN).

The following observations on this subject in two young children are communicated here as they also present some points of clinical and bacteriological interest.

I. The boy W. was admitted to the Babies Department of the Wilhelmina Hospital at Amsterdam in November 1933, at the age of 4 $^1/_2$ months. He was the first child of a healthy father. The child's mother, at the time of admittance of the baby, was nursed for pulmonary tuberculosis already for about two months and the history learned that the infant had been exposed during the first two months of life to infection, as it was breast fed by the mother during that time. The general condition of the boy was favourable, the temperature only during the first weeks after admittance to the hospital slightly elevated. At physical examination there was dullness over the right upper lobe; weakened breath sounds were heard over the lower half of the right lung and many coarse bronchitic murmurs could be heard over both lungs. Spleen palpable. The blood picture showed a distinct shift to the left. The sedimentation rate was clearly increased. The tuberculin reaction was positive. On the first roentgenogram a fairly dense elliptic lesion was visible in the right lower lobe surrounded by an extensive perifocal zone of reaction. As already could be derived from the clinical symptoms (typical expiratory and inspiratory stridor) the roentgen picture showed an extensive swelling of the tracheobronchial and hilum glands. The condition of the baby gradually improved, the stridor disappeared. The sedimentation rate of the erythrocytes already after a few months had decreased to normal values. No anemia.

Eight months later, when the infant was one year old and the perifocal reaction had already disappeared for several months, calcification of the focus started. The focus then was as large as a plum and sharply demarcated. During the following months the calcification, which had a mottled aspect, became more and more dense (fig. 1, Febr. 1935). In Aug. 1935, when the child was discharged from the hospital, the decrease of the primary focus had already begun (fig. 2). At regular control visits the roentgen examination learned that the focus gradually became smaller (fig. 3, July 1936). Signs of calcification in the hilum glands did not appear till one year after the first observation. With exception of a very moderate growth the general condition remained good. In Aug. 1936 he had measles.

Fig. 1.



Schema of the decrease in size of the calcified primary focus in Case I.

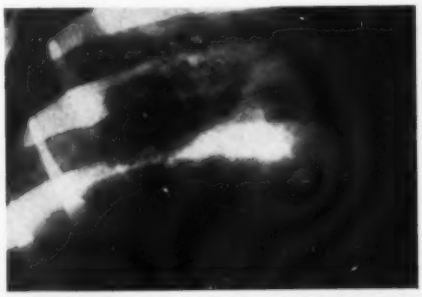


Fig. 2.

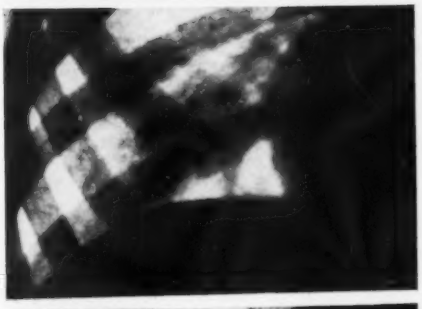


Fig. 3.

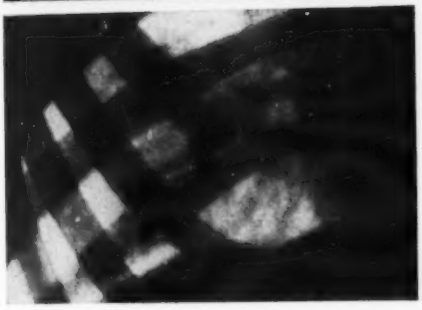


Fig. 4.

In the summer of 1937 the child was taken into the hospital for scarlet fever. The roentgen examination of Oct. 1937 showed further decrease of the calcification of the primary focus (fig. 4). After his discharge he started coughing. In Dec. 1937 temperature and sedimentation rate of the erythrocytes were slightly elevated. There was swelling of cervical glands. At physical examination of the lungs no particularities were found. The roentgen picture showed swelling of the left hilum, some calcified spots in both hili, small calcium deposits at the place of the original primary focus surrounded by a rather diffuse, not very large shadow, extending to the right hilum but especially laterally and downwards.

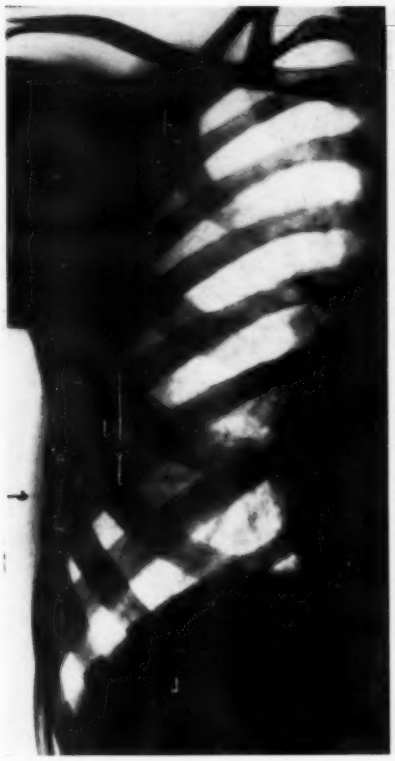


Fig. 5.

Fig. 6.

Probably we had to do here with a flaring up of the process after scarlet fever with new perifocal infiltration.

In Jan. 1938 the child was admitted to the Children's Sanatorium »Hoog-Blaricum». The boy remained there till Febr. 1939; the general condition improved. Symptoms of activity failed. On the roentgen picture taken in Nov. 1938 there was swelling of both hili with some dense calcified spots and only a *trace* of the calcified primary focus covered by a rib was still visible (fig. 5). In March 1941 the general condition was excellent. Since his discharge from the sanatorium the boy has never been ill. On the roentgen picture of the lungs of March 1941 *no trace of the original calcified focus* could be found (fig. 6). In the right hilum a single calcified spot was still visible and further several fibrous strands from the right hilum to the lower part of the right lung.

The accompanying photo's and scheme give an idea of the decrease in size of the focus in this case.

Examination of the fasting stomach content for the presence of tubercle bacilli (guinea-pig test) has repeatedly been performed in this case with intervals. Since the first examination in Nov. 1933 positive results were obtained for several years; the last

Fig. 7.

Fig. 8.

positive one dates from Aug. 1938. Since then twice (in Nov. 1938 and in Febr. 1939) the test has been negative. The general condition of the boy and the results of the radiological and bacteriological investigation give reason to regard the boy as cured since Febr. 1939.

II. The second case was that of the girl E., fourth child of a mother suffering from pulmonary tuberculosis. The first child died of meningitis, the second one of convulsions, the third one is healthy. Our patient was born in March 1936 and at birth got Calmette's vaccin; the child remained in close contact with the mother during the first 6 months of life. When taken into the Paediatric Clinic at the age of 8 months, the girl had been coughing for some weeks. There was slight dullness under the right scapula. The v. Pirquet test was highly positive. The roentgen examination showed a triangular infiltration in the right lung close to the right hilum, and swelling of the paratracheal glands on the same side. The child remained in the hospital for 8 months; recovery took place gradually, without complications. The deviations at physical examination disappeared. For a short time the spleen was slightly palpable. Due increase in weight occurred some months after admittance. The temperature always was normal, with exception of a short period some weeks after the admittance. The sedimentation rate of the red blood corpuscles gradually decreased, and the blood picture lost its toxicity. Also the roentgenological deviations decreased. At discharge from the hospital there was a pulmonary nodule at the place of the original infiltrate close to the right hilum, showing beginning calcification (fig. 7). From the fasting stomach content human tubercle bacilli were cultivated. From the hospital the child went to the Children's Sanatorium »Hoog-Blaricum»[1] and remained there for about 8 months. The general condition improved. The temperature oscillated during the stay in the sanatorium; the child got scarlatina. Culture and guinea-pig test with the fasting stomach content performed respectively 2 and

[1] Our thanks are due to dr. HUET, direktor of the sanatorium, who drew our attention to this case and allowed us to make use of the histories.

Fig. 9.

6 months after admittance to the sanatorium both gave a negative result. The roentgen picture taken in April 1938 revealed a fairly dense calcified nodule at the right side above the hilum (fig. 8).

In June 1941 the child was again taken into the sanatorium. Since she discharge in 1938 she has had measles and parotitis; for the rest she remained well, only slight coughing during last weeks. She is a lean delicate child; no deviations at physical examination, no signs of activity of the former tuberculous process. Roentgenological examination showed that the *calcification* near the right hilum *nearly totally has disappeared* (fig. 9). There also is no trace of calcified hilar glands. The v. Pirquet test is positive.

Comment

The observation of these two cases once more indicates that calcifications in primary pulmonary tuberculosis in childhood may sometimes disappear within some years so that roentgenologically signs of the former tuberculous process are already absent even before puberty is reached. One could object that in our two cases we have not to do with calcifications of the pulmonary focus, but then we want to remark that one is accustomed in roentgenology to regard pictures as present in these cases always as a sign of calcification.

In the first case the roentgenological disappearance of the calcifications in the primary focus, after having passed the different stages of development, occurred in the course of seven years. Four years after its first appearance only a trace of the calcification could still be found. In the second case the practically total disappearance of the deposits of calcium occurred within four years after its first appearance.

The two cases, both starting in early infancy, were further characterized by the unexpected favourable course and a fairly early arise of signs of calcification.

In the series of 158 cases of intrathoracic tuberculosis in infants studied by BRAILEY, the youngest patient in whom calcification was

observed, was ten months old. This infant, like our first patient, had been exposed to infection for the first month of life; the tuberculin reaction was already positive at six weeks of age.

In our first case tubercle bacilli could no longer be cultivated from the fasting stomach content when roentgenologically only a trace of calcification of the primary focus could still be found. In the second case tubercle bacilli could already no longer be cultivated a few months after the calcification of the primary focus had started. In this latter case occurring in an infant which had obtained Calmette's vaccin at birth, the bacilli which formerly were cultivated from the fasting stomach content, were of the human type.

In the first child no tuberculin test was done after the disappearance of the calcification; so we cannot say in how far in this case, by exception, the allergy is lost in the same time as the calcification has disappeared. The second child recently reacted positively to tuberculin.

SUMMARY

Description of two cases of lung tuberculosis in young infants. The calcification of the primary focus started fairly rapidly in both cases. The calcification after having passed different stages of development, decreased in such a way that after some years in the first case no trace of it was visible on the roentgenogram, whereas in the second case only a small rest remained. Tubercle bacilli in the first case no longer could be cultivated from the fasting stomach content when roentgenologically the calcification of the primary focus had disappeared. In the second case the culture was already negative a few months after the calcification of the focus had started.

ZUSAMMENFASSUNG

Beschreibung zweier Fällen von Lungentuberkulose bei Säuglingen; bei beiden fing die Kalzifikation des primären Herdes schon bald an. Nachdem sie die verschiedenen Phasen der Entwicklung passiert hatte, bildete die Kalzification sich zurück im Verlaufe einiger Jahre bis sie im ersten Falle schliesslich ganz verschwunden war, während im zweiten Falle nur ein ganz kleiner Rest auf dem Roentgenbilde sichtbar blieb. Im ersten Falle konnten aus dem Mageninhalt keine Tuberkelbazillen mehr gezüchtet werden, als im Roentgenbilde die Kalzifikation des primären Herdes verschwunden war. Im zweiten Falle war diese Kultur schon negativ einige Monate nachdem die Kalzifikation des primären Herdes angefangen hatte.

RÉSUMÉ

Description de deux cas de tuberculose pulmonaire chez de petits enfants. La calcification de la lésion primaire avait commencé assez tôt dans les deux cas. Cette calcification, après avoir passé les différents stades du développement, diminuait au cours de quelques années d'une telle manière que dans le premier cas elle disparaissait tout à fait à la radiographie, tandis que dans le second il ne restait finalement qu'un minuscule point. Dans le premier cas les bacilles de Koch ne pouvaient plus être cultivés du

contenu de l'estomac pris à jeun quand la calcification de la lésion primaire avait tout à fait disparu sur la radiographie. Dans le second cas la culture était négative déjà quelques mois après le commencement de la calcification de la lésion primaire.

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FROM THE ORTHOPEDIC CLINIC OF KAROLINSKA INSTITUTET, STOCKHOLM (PROFESSOR H. WALDENSTRÖM) AND THE NYNÄS SANATORIUM (DR F. SUNDELIN)

THE VACUUM PHENOMENON IN THE INTERVERTEBRAL DISCS[1]

by

Folke Knutsson

In certain cases the so-called true joint-seam in a joint appears as a thin air-streak between the articular surfaces. It can thus be regularly provoked in the shoulder-joint of a child by hyper-extension, and can be made to disappear immediately if the degree of extension is diminished. In a similar way it can be provoked by such strong traction in a finger-joint that the contact between the articular surfaces is broken. In joints with osteoarthritis, where the articular surfaces are more or less incongruent, it can be provoked in the same way, when in certain positions parts of the articular surfaces lose contact with each other. A study of this phenomenon, with an account of the descriptions of it to be found in roentgenological and anatomic literature, has been made by W. MAGNUSSON. The phenomenon is due to the generation of such pressure in the joint that the synovial fluid becomes vapourized and gases that exist in solution in the synovial fluid are changed to the gaseous form. The joint space, when thus filled with gas, appears on the roentgenogram as a thin air-streak. If the pressure is diminished by diminishing the hyper-extension or the traction or by re-establishing the congruency between the articular surfaces the air-streak disappears at once. It is thus apparent that we are here confronted with a vacuum phenomenon, and I shall so refer to it in the following.

MAGNUSSON exemplifies his thesis with a number of joint cases and also describes cases with a similar air-streak in an intervertebral cartilage in spondylitis deformans and in symphysis in connection with gravidity. He concludes his work by asserting that the phenomenon is chiefly of theoretical and not practical importance.

In the course of my work as roentgenologist at The Orthopedic Clinic and The Nynäs Sanatorium I have in connection with a number of back

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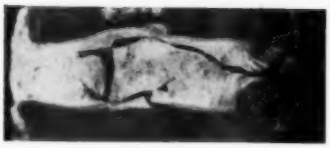


Fig. 1. Disc-degeneration (osteochondrosis) with crack-formations in degenerated disc-substance (After JUNGHANNS: Die Pathologie der Wirbelsäule. Hb d. spez. Path. Anat. u. Hist. 1939 (HENKE-LUBARSCH)).

examinations been in a position to observe the vacuum phenomenon, and have found that in certain cases it may be of practical importance. I have found vacuum phenomena of two radically different kinds in conformity with the patho-anatomical changes that are found in cases of disc-degeneration (osteochondrosis) and spondylitis deformans. I base my remarks in this connection on the descriptions given by SCHMORL and his school, and I try to keep these two concepts distinct, well knowing that changes of these two kinds often occur simultaneously in one and the same cartilage-disc.

The vacuum phenomenon in cases of disc-degeneration. In cases of disc-degeneration degenerative changes appear centrally in the disc-substance, originating from the nuclear region. The disc-substance dries up and at the same time irregular cracks appear. The process may finally lead to complete disintegration of the disc. The peripheral part that consists of annulus fibrosis, however, remains intact. (Fig. 1).

In conformity with this patho-anatomical basis, the vacuum phenomenon in cases of disc-degeneration is characterised by irregular air-streaks that as a rule run centrally in the disc-substance parallel with the surfaces of the vertebra. They do not reach the periphery of the disc. Obviously, a vacuum arises in these dry crack-formations as a result of such movements between the vertebrae as cause the walls of the crack to gape apart. In a healthy disc, on the other hand, where preformed crack-formations do not exist, the phenomenon obviously cannot arise. Vacuum phenomena of this kind are thus pathognomonic for disc-degeneration, and apart from calcifications they constitute the only roentgenological symptom that can be referred directly to the disc-substance. (Figs. 2, 3, 6).

The roentgen diagnosis of disc-degeneration is otherwise based upon secondary changes, to wit, a decrease in the height of the intervertebral cavity, as well as sclerosis of the surfaces of the vertebrae and labial formations at their edges. One also often finds reciprocal displacement of the vertebrae, especially a rearward dislocation of the upper of two vertebrae (retro-position). In cases where these secondary changes are absent and the intervertebral cavity has a normal appearance the vacuum phenomenon constitutes the only roentgenological symptom, and is then clearly of practical value. (Figs. 3 and 6).

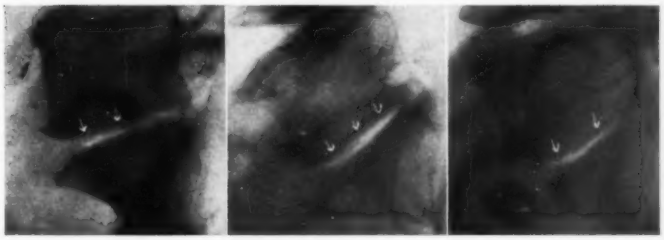


Fig. 2. Three cases of disc-degeneration with long vacuum phenomenon indicating preformed crack-formations. These do not reach the periphery of the disc, which agrees with the circumstance that the outer part of annulus fibrosus is intact. The intervertebral cavities have diminished height. The surfaces of the vertebrae show reactive sclerosis and labial formations at their edges. These skeletal changes enable one to diagnose disc-degeneration, and the vacuum phenomenon in these cases constitutes only a secondary find.

The vacuum phenomenon in spondylitis deformans: In spondylitis deformans the anatomical change takes the form of a cracking and falling away of parts of the periphery of annulus fibrosus from the point of attachment to limbus vertebre while the central part of the disc-substance with nucleus remains intact. Through this breaking-off, which may involve a greater or lesser part of the ambiance of the disc, the barrier is broken and the consequence is protrusion of the disc and prolapse of its inner parts. The protruding disc exerts a pressure on lig. longitudinale, and the increased tension in this ligament leads to osteophytic accretions at its point of attachment on the cylinder surface of the vertebra at a short distance from the vertebral edge. (Fig. 4).

In one single case I have found a vacuum phenomenon that reflects this anatomical basis. (Fig. 5). At the vertebral edges of L. III and L. IV there was a vacuum-bubble at least the size of a pin's head, situated immediately next to the surface of the vertebra quite near the anterior edge. It is thus so situated as to correspond in position to the spot where the crack-formation in annulus fibrosus in cases of spondylitis deformans occurs. (Fig. 4). In this case there were no skeletal spondylitis deformans changes but only typical change in the disc-substance. The vacuum phenomenon thus constituted in this case an initial symptom of spondylitis deformans.

Besides the morphological basis of the vacuum phenomenon I have also studied its mechanical aspect. In fig. 5 a the patient is lying on the photographing-table in the usual lordotic position on the side. The other picture was taken after the patient had been lying in the same position for 15 minutes. The third picture (c) was taken immediately

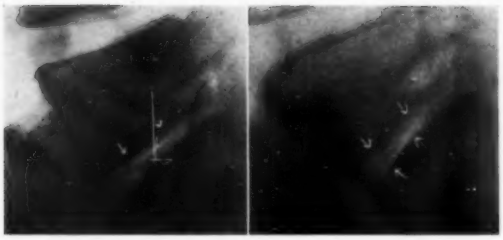


Fig. 3. Two cases of disc-degeneration with typically centrally situated crackformation that has given rise to the vacuum phenomenon. The crack is not continued into the periphery. In these cases the intervertebral cavity is in other respects intact, and the surfaces of the vertebrae show no secondary changes. The diagnosis of disc-degeneration is thus in these cases based only upon the vacuum phenomenon, which is here of practical importance.

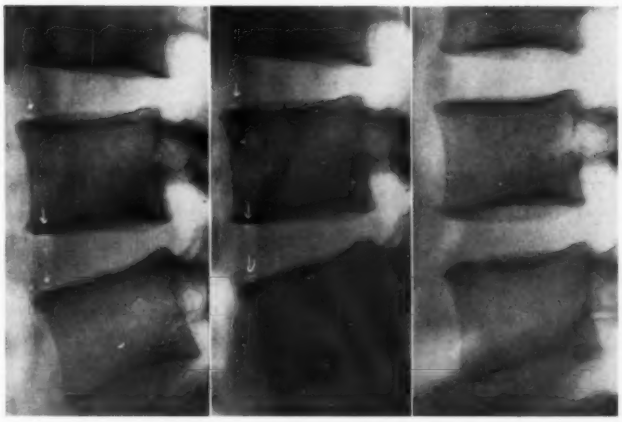
Fig. 4. Incipient spondylitis deformans. At s there is a crack-formation in annulus fibrosus near the edge of the vertebra. (After JUNGHANNS: Die Pathologie der Wirbelsäule. Hb d. spez. Path. Anat. u. Hist. 1939 (HENKE-LUBARSCH)).

after the patient had assumed the kyphotic position. The vacuum phenomenon thus remains unchanged for at least 15 minutes, disappearing immediately upon assumption of the kyphotic position, when the gaping of the walls in the crack-formation ceases and the walls are brought into contact with each other.

The same relation is illustrated in fig. 6. The first picture (a) was taken in the lordotic position, (b) in the kyphotic and (c) immediately afterwards in the lordotic position again. The vacuum phenomenon is thus found in the lordotic position but disappears in the kyphotic position.

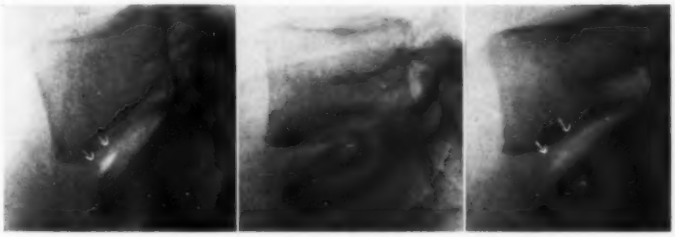
In fig. 7 (chondrodystrophia) one observes clearly considerable disturbances in the disc-substance with preformed crack-formations. The first picture (a) was taken in the lordotic position, (b) 15 minutes afterwards, with position unchanged and (c) immediately after assumption of the kyphotic position.

These experiments thus show that the vacuum phenomenon appears immediately upon assumption of a position of the lumbar spine (lordosis) that causes the walls of the preformed crack-formation to gape apart. The phenomenon remains for at least 15 minutes and probably consid-



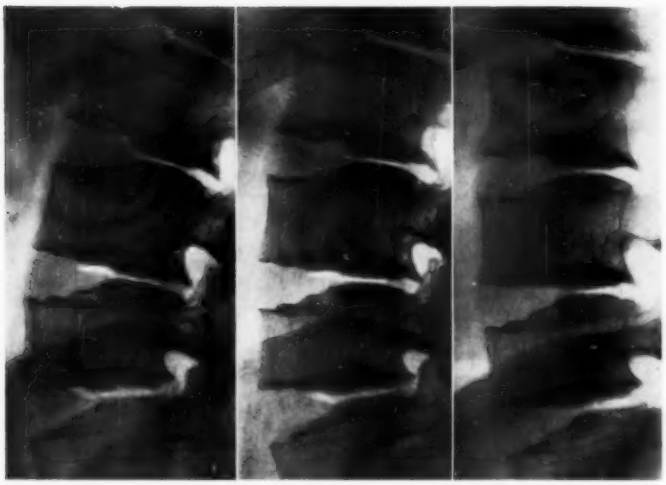
a, b. c.

Fig. 5. a. habitual lordosis, b. after 15 minutes in the same position, c. immediately after assumption of the kyphotic position. A small vacuum-bubble quite near the surface of the vertebra at the anterior edge, corresponding to the point of attachment of the annulus. The vacuum phenomenon remains for at least 15 minutes and disappears immediately upon assumption of the kyphotic position. No skeletal spondylitis deformans changes. The character of the vacuum phenomenon justifies the diagnosis of incipient spondylitis deformans.



a. b. c.

Fig. 6. a. in the lordotic position, b. in the kyphotic and c. immediately after resumption of the lordotic position. The vacuum phenomenon appears in the lordotic position and disappears in the kyphotic position. The intervertebral cavity is in other respects normal, and the surfaces of the vertebrae show no reactive changes. The diagnosis of disc-degeneration is in this case based exclusively upon the vacuum phenomenon.



a. b. c.

Fig. 7. Osteochondrodystrophia with preformed crack-formations in the disc-substance. a. in lordosis, b. 15 minutes afterwards in the same position, c. immediately upon assumption of the kyphotic position. The vacuum phenomenon appears in lordosis and disappears almost completely in kyphosis.

erably longer if the position is maintained unchanged, which indicates that the substitution of fluid for the gaseous content of the crack-cavity is an extremely slow process. As soon as the stretching of the crack is relieved by assumption of the kyphotic position, which causes the walls of the crack to be pressed together, the vacuum phenomenon disappears.

SUMMARY

Crack-formations in the intervertebral discs may sometimes manifest themselves on roentgen examination thanks to a vacuum which makes them appear as thin air-streaks in the intervertebral space (the vacuum phenomenon). This vacuum phenomenon takes two radically different forms that may be referred to the patho-anatomical conditions in spondylitis deformans or in disc-degeneration (pathognomonic symptom). A positive vacuum phenomenon may exist before the development of skeletal changes and thus justify an early diagnosis.

ZUSAMMENFASSUNG

Risse in den Intervertebralscheiben können sich zuweilen bei der Röntgenuntersuchung offenbaren, nämlich infolge eines Vakuums, das sie als dünne Luftstreifen im Intervertebralraum erscheinen lässt (Vakuumphänomen). Dieses Vakuumphänomen

tritt in zwei durchaus verschiedenen Formen auf, je nachdem die pathologisch-anatomischen Verhältnisse der Spondylitis deformans oder der Osteochondrosis vorliegen (pathognomonisches Symptom). Ein positives Vakuumphänomen kann bereits vor der Ausbildung von Skelettveränderungen bestehen und so eine frühe Diagnose ermöglichen.

RÉSUMÉ

Les fissures au niveau des disques intervertébraux peuvent parfois se manifester à l'examen radiologique par un vide qui les fait apparaître comme de minces traînées d'air dans l'espace intervertébral (le »phénomène du vide»). Ce phénomène du vide prend deux formes radicalement différentes qu'on peut attribuer aux différences anatomo-pathologiques existant entre la spondylite déformante d'une part et la dégénérescence discale de l'autre (symptôme pathognomonique). Un phénomène du vide peut être positif avant le développement d'altérations squelettiques et asseoir ainsi un diagnostic précoce.

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FROM THE ROENTGEN CLINICS OF THE VIBORG TOWN AND COUNTY HOSPITAL AND THE KJELLERUP HOSPITAL (CHIEF: KRISTIAN OVERGAARD, M. D.)

A CASE OF PARANEPHRITIC ABSCESS WITH CHARACTERISTIC PYELOGRAM[1]

by

Kristian Overgaard

The value of roentgen examination in cases of renal and pararenal abscesses is generally recognised. As a rule, it is practiced in the form of simple radiography without the use of contrast medium, and in the pictures obtained in this manner the effacement of the renal and psoas contours and the concave lumbar scoliosis are very valuable criteria. According to SHANE, HOWARD and HARRIS, the first of these symptoms is almost constant in cases of pararenal abscess, while in other renal affection it is present only in about 30 per cent of cases. Scoliosis, according to the same authors, is present in about 45 per cent of cases of pararenal abscess. The pleural exudate, too, is a not unimportant sign of such a disease. According to OCHSNER and GRAVES it is found in 22 per cent of all cases of subdiaphragmatic abscesses, and NESBIT and DICK found it in 16.5 per cent of cases of perirenal abscess. The frequency and degree of development of the pleural changes vary considerably, however, and depend to a great extent on how long the disease has been in progress. In some cases, though, they are so pronounced that they completely obscure the actual focus.

To refrain from employing pyelography in these affections is by most urologists regarded as showing excessive cautiousness, and BOEMINGHAUS, especially, recommends this method of examination. In a considerable number of cases it will enable one to demonstrate changes in the renal pelvis that must be supposed to be primary for the affection, such as pyonephrosis or tumors, or to ascertain the existence of a connexion between the renal pelvis and an abscess cavity. Also a displacement of the kidney and some deformation of the pyelogram will it often be possible to demonstrate.

[1] Submitted for publication Oct. 29, 41.

If there is an abscess in the kidney itself — a nephrocarbuncle — the pyelogram will be seen to be deformed in the same manner as in the case of a tumor formation (HOHLBAUM), and the difficulty of the differential diagnosis between a tumor and an abscess is mentioned by several authors (BOEMINGHAUS, BOSHAMMER, SCHEELE and TESCHENDORFF).

It is only recently that it has been noticed that also abscess formations in the pararenal space are capable of producing pyelograms resembling a kidney tumor, apparently without the existence of any focus in the kidney itself. Thus, DEUTICHE (1940) reports 6 cases of pararenal abscesses the pyelograms of which strikingly resemble kidney tumors, and a couple of cases reported by JUNKER (1937) show similar features.

As these facts seem to be little known, the following case may be of interest.

On May 11th, 1940, a girl, aged 15, was admitted to the Kjellerup Hospital. Except for a slight dysuria when she was about 12 years old, she had always been in good health until, on April 20th, she suddenly had become ill, with temperature 39° and an indefinite pain in the abdomen, especially in the right side, radiating out towards the flank and the lumbar region. There was no cough or vomiting; but a slight dysuria, which soon disappeared. The examination at her home showed no tenderness or swellings either in the abdomen or in the lumbar region, nor any other focal symptoms. In spite of sulfanidamide treatment her temperature remained steadily around 38—39°. Widal's reaction was negative. At her admission there were no signs of focal affections. Stethoscopy showed normal conditions. The abdomen was natural, without tenderness or tumefactions. Urine, normal. Temperature, 39.9. Sedimentation reaction, 110 mm./h.. Roentgen examination of the thorax showed normal conditions.

During the following months the patient lay febrile, with a temperature that from about 39° gradually fell to a little over 38°. The clinical examination failed to reveal any signs of abdominal processes, but already on May 18th there were signs of a right-sided pleurisy. These were confirmed by a *roentgen examination* on May 26th, which showed a medium-sized exudate in the right pleura. By puncture a mottled, greenish fluid was obtained, which on cultivation did not show growth of bacteria. On June 24th, a great increase of the exudate and some displacement of the heart and mediastinum towards the left were found. About 800 c. c. of fluid was withdrawn by puncture, and from then on there was a great diminution in the quantity of exudate. The case was judged to be one of exudative pleurisy, but as the Mantoux reaction in spite of repeated tests continued to be negative a suspicion arose that the pleural affection might be secondary to an abdominal process. This suspicion was strengthened by the fact that the diaphragm shadow stood about 1 to 1.5 intercostal space higher on the right than on the left side. But beyond this the clinical examination did not show any signs of pathologic changes in the abdomen or the kidney, and not until October 22nd was a *roentgen examination* made of *the abdomen and the urinary tract*. This examination showed a slight sinistroconvex lumbar scoliosis and effacement of the right psoas shadow and renal contour whereas the contour of the right flank was distinctly stratified and the contours of the left psoas and kidney natural. There were no signs of abscess formations between the intestines; the liver shadow was natural. These findings were interpreted as signs of a pararenal abscess, and on Oct. 25th a *urogram* was therefore taken, which on the left side showed a fairly natural renal pelvis, while on the right side the filling was defective. *Pyelographic examination* on Nov. 1st showed a natural renal pelvis on the

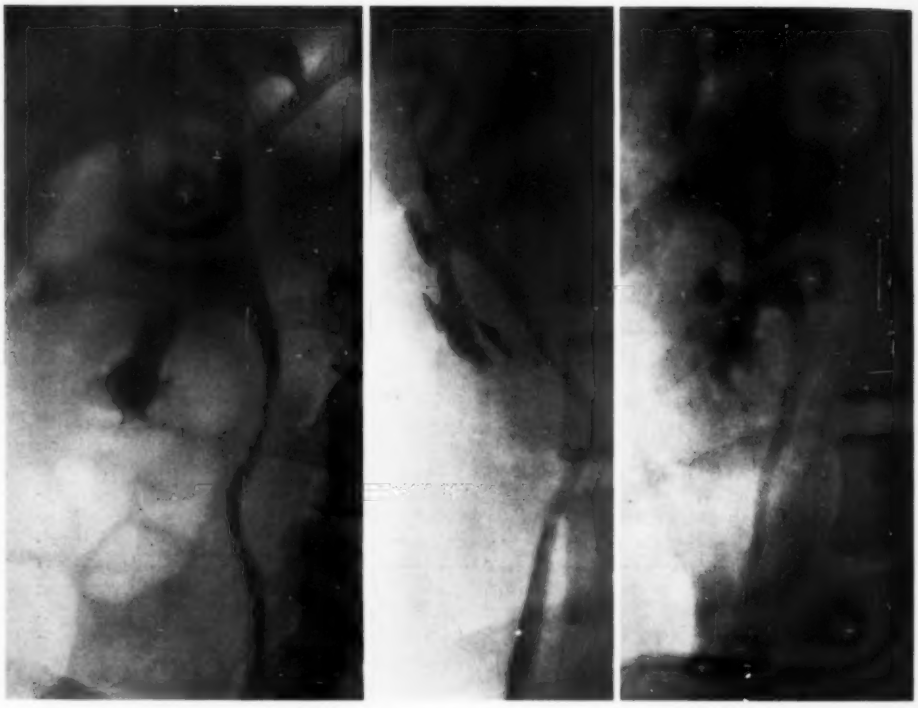

Fig. 1. Fig. 2. Fig. 3.

left side. On the right side (Fig. 1) the upper calyces were only sparsely filled, were distinctly elongated and spread apart, and the individual papillæ were slightly cup-shaped. Sideviews (Fig. 2) showed a distinct forward displacement of the renal pelvis, which was very much flattened and formed an anteroconvex arc. The whole picture thus showed the changes characteristic for an intrarenal tumor in the posterior part of the kidneys, but in view of the pleural changes and the effaced renal and psoas contours the case was diagnosed as intrarenal abscess with perirenal propagation, subsidiarily as pararenal abscess.

During the following time, the patient continued slightly febrile; her appetite was poor, she vomited a little, and became thin. She had occasional spells of pain in the lumbar region, but there was no actual dysuria. There was no positively demonstrable tumefaction about the right kidney, but its inferior pole could be felt. The inferior margin of the liver extended two fingers' breadth below the curvature. There was a little albumin in the urine (0.01 per cent), a few erythrocytes and a few leukocytes.

On Dec. 10th, the patient was operated on (Senior Surgeon, Dr. DALSGAARD). A lumbar incision was made in the right side, and below the muscle was found a lardaceous abscess membrane, which closed an abscess cavity about as large as a child's head. When this was opened the kidney could not be seen. After two drains had been placed, the wound was closed. A smear preparation of the pus showed staphylococcus aureus.

After the operation, the patient's temperature soon became normal, her general condition was good and she ate well. For a long while there was considerable secretion from the wound, but this gradually became less, and by June 1st, 1941 the fistula was closed.

A urogram taken Feb. 11th, 1941, (Fig. 3), showed that the shape of the right renal pelvis was now natural, but the excretion markedly slighter than on the left side. On April 8th, 1941, the patient was discharged in good health. There was a slight albuminuria and *a few red and white blood corpuscles.*

A follow-up examination on Aug. 21st, 1941, showed the patient in full health and working capacity. Objectively, her condition was natural. Urine: + alb. (0.02 per cent). Microscopy: natural. *Urography:* renal pelvis perfectly natural on both sides; excretion strongest on the left, however.

Both clinically and roentgenologically, this case thus shows the changes typical for a late recognised pararenal abscess. Especially noticeable is the deformation of the renal pelvis found by the pyelographic examination. According to our experiences hitherto, this deformation must be considered as expression for an intrarenal process — tumor or abscess — that bursts the calyces apart; but neither in the operative findings nor in the subsequent course was there anything that pointed to the existence of an intrarenal focus. This agrees exactly with DEUTICHE's observations, when he in 6 cases of pararenal abscess found a greater or lesser displacement of the renal pelvis in one direction or other, turning and tilting of the cavity system about all its axes, compression of the system, filling defects, and deformation of the calyces as well as changes in their position in relation to each other. On roentgen examination after the abscess had been drained, he in all cases found a normal renal pelvis, and he conludes from this that the pressure of this extrarenal process is capable of producing these changes. He was further confirmed in this supposition by the results of a series of experiments with removed kidneys, in which he found that there by a slight pressure from the outside could be produced precisely similar changes in the shape of the renal pelvis.

SUMMARY

The author reports a case of pararenal abscess formation, in which the pyelogram showed the changes characteristic for an intrarenal tumor. Pyelograms taken after the disease was past showed normal conditions. These findings confirm DEUTICHE's observations in regard to the roentgenologic picture of the pararenal abscess.

ZUSAMMENFASSUNG

Verf. berichtet über einen Fall von pararenalen Abszess, wo das Pyelogramm die für einen intrarenalen Tumor charakteristischen Veränderungen zeigte. Nach Ablauf der Erkrankung aufgenommene Pyelogramme zeigten normale Verhältnisse. Diese Befunde bestätigen DEUTICHES Beobachtungen hinsichtlich des Röntgenbildes bei pararenalem Abszess.

RÉSUMÉ

L'auteur rapporte un cas d'abcès pararénal où le pyélogramme montrait les altérations caractéristiques d'une tumeur intrarénale. Les pyélogrammes établis après guérison faisaient voir un état normal. Ces constatations confirment les observations de DEUTICHE concernant l'image radiologique de l'abcès pararénal.

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FROM OPLANDS FYLKESSYKEHUS, LILLEHAMMER, NORWAY (SURGEON-IN-CHIEF: E. MURSTAD), DEPARTMENT OF ROENTGENOLOGY (CHIEF: KRISTIAN ANDRESEN)

DUODENAL STENOSIS AS A COMPLICATION TO GALL-STONES[1]

by

Bjarne Andersen

A spontaneous interior gall fistula is a relatively unusual occurrence, but during the last years a number of papers on the roentgenological diagnosis of these fistulæ have been published, also in this journal (GRÅBERGER, LÖNNERBLAD, and others).

The fistulæ may form a connexion between the biliary ducts and practically speaking all other organs (the stomach, duodenum, ileum, colon, appendix, the renal pelvis, the urinary bladder, and even the pericardial cavity). Most often a connexion between the gallbladder and the intestinal canal is formed, and the cholecysto-duodenal fistula is the most common kind of interior gall fistulæ. The fistulæ allow even large gall-stones to pass through to the intestine where they may give rise to an ileus. This latter condition is comparatively rare. JUDD & BURDEN found 1 case of ileus caused by gall-stones in 153 cases operated upon on account of interior gall fistula (cited from WAUGH).

On going through the literature on the subject, several records are found of gall-stone ileus as a consequence of intestinal occlusion *below* the duodenum showing the ordinary roentgenological aspects of ileus in the small intestines. (SCHÉLE, SÄFWENBERG, and others). A stenosis caused by gall-stones *higher up*, in the duodenum, however, seems to be more rare. CRANE has found that, during the years 1923—31, only 4 cases have been published: he, furthermore, records 1 case which he, himself, has observed. This was a man aged 80 years, who had a gall-stone in the duodeno-jejunal flexure and a fistula between the gall-bladder and the duodenal bulb. The diagnosis was made roentgenologically and the patient was operated upon, but he died two days later.

[1] Submitted for publication Jan. 17, 1942.

WAKEFIELD, VICKERS & WALTERS, of the Mayo Clinic, record 10 cases of gall-stone ileus. In 3 cases the obstruction was located to the duodenum; in one case the diagnosis was made at the postmortem, in two others at the surgical operation.

WAUGH has described 1 case — a man, 72 years of age, who was operated upon after the clinical and roentgenological diagnosis — duodenal ulcer with stenosis — had been made. A fistula between the gall-bladder and the duodenum was found, likewise a stenosis in the duodenal bulb caused by two gall-stones; there were also numerous stones in the gall-bladder.

I have not found that any roentgen picture has been published in the literature at my disposal; I, therefore, consider the following case to be of interest:

The patient was a woman, 65 years of age; she was an inmate of Oplands Fylkessykehus from 16. 9. 1940 up to 21. 10. 1940.

She had not previously had any serious disease with the exception of an infection of the unrinary tract 5 years ago. For about 10 years she had suffered from a not characteristic dyspepsia, feeling distended and inflated after eating meat, cabbage, fresh fruit, etc. She had never had any actual pain in the stomach and had not suffered from any attack similar to those caused by gall-stones. Always constipation; never any signs of blood in the fæces. Good appetite; no loss in weight. The last 14 days before admission her digestive troubles increased. She had much rumbling in the stomach, a feeling of nausea, and lost her appetite. 3 days before admission she vomited about 2 litres of a light-coloured, yellow fluid containing no old food remnants. She had since then only taken liquid food, but had had similar vomitings all the same .

On physical examination the patient was thin and delicately built; she was greyish pale, but in good condition otherwise. The abdominal wall was thin, the relief of an extended stomach with »splashing» could be clearly distinguished. No visible peristalsis of the stomach. No palpable tumor.

95 per cent hæmoglobin. Erythrocyte sedimentation rate was 20 mm. in 1 hour. Fæces — Benzidine test was positive on two occasions, and negative once. Ewald's test meal — 240 c. cm. HCl/TA — 12/54.

Roentgenological Examination of Stomach and Duodenum

The stomach was large and flaccid, the outlines soft and even, no sign of niches or infiltrations.

The duodenal bulb (Fig. 1) would not fill properly. A defect the size of a dove's egg was seen surrounded by a brim of contrast medium. Laterally above the large defect some smaller defects were also noted No tumor could be palpated during radioscopy.

With regard to the *diagnosis* it lies near to consider a *tumor*. The roentgenological aspect and the anamnesis when taken together, might indicate a *benign* tumor. However, benign tumors in the duodenal bulb are sheer curiosities (ALBRECHT): 30 such cases in all have so far been

published. Papillomata are the most common (ÅKERLUND). *Malignant* tumors in the duodenal bulb are, if possible, even more rare. The malignant tumors in the duodenum generally commence at Vater's papilla. It, therefore, seems hardly possible that the patient should suffer from a tumor in the duodenal bulb. — She might have a polypous tumor in the canalis of the stomach, with polyps protruding through pylorus into the bulb. — The roentgenological examination was repeated to try to confirm the latter hypothesis; however, the canalis seemed to be normal.

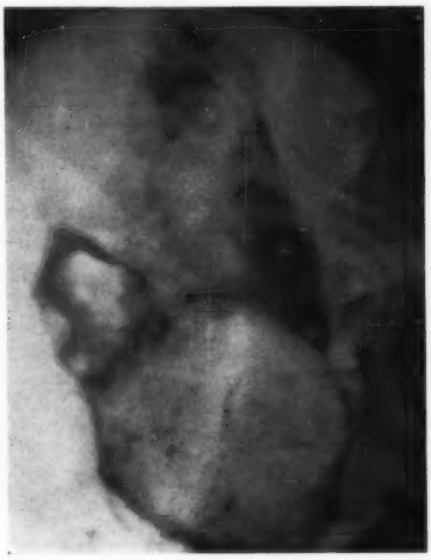

Fig. 1.

A foreign body in the duodenal bulb was not inconceivable; this could not possibly have arrived from anywhere outside, it would, in case, have to be a gall-stone which might have arrived there through an interior gall fistula. This eventuality was mentioned during the discussion of the case, but it was dropped again. The possibility could not be excluded only because the patient had not had any biliary colic, but the age of the patient and her occult intestinal bleedings made it most likely to expect the presence of a tumor.

The patient suffered from retention in the stomach, and the indication for operation was thus clear. Laparatomy and duodenotomy were

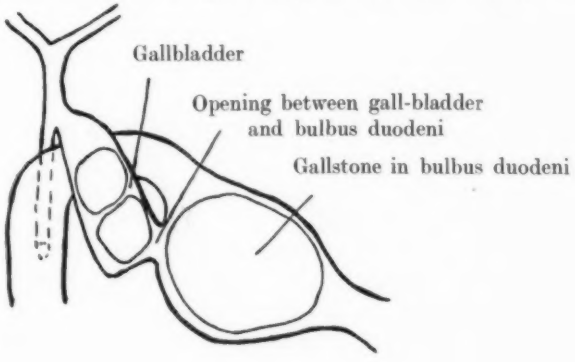

Fig. 2.

performed. At the duodenotomy a gall-stone (mixed stone) the size of a plum, slipped out by itself: two smaller stones were also removed from the gall-bladder.

Between the gall-bladder and the duodenal bulb there was a wide opening (Fig. 2), and the bulb was thus continued in two equal passages the lower of which was the gall-bladder. The surgeon restricted the operation to the removal of the stones, and closed the wound in the bulb without removing the gall-bladder or performing a gastroenterostomy. The postoperative period was uneventful. The patient was discharged after 4 weeks, she had then no pain in the stomach, no nausea, and no vomiting. An examination carried out 1 year after the operation proved the patient to be in good health.

SUMMARY

The author records one case of internal gall fistula — a cholecysto-duodenal fistula — in a woman 65 years of age. A gall-stone, the size of a dove's egg, filled the duodenal bulb and caused stenosis.

ZUSAMMENFASSUNG

Verf. berichtet über einen Fall von innerer Gallenfistel, eine Cholecysto-Duodenal-Fistel, bei einer 65-jährigen Frau. Ein Gallenstein von der Grösse eines Taubeneis füllte den Bulbus duodeni und bewirkte Stenose.

RÉSUMÉ

L'auteur relate un cas de fistule biliaire interne — fistule cholécysto-duodénale — chez une femme de 65 ans. Un calcul biliaire, de la taille d'un œuf de pigeon, remplissait le bulbe duodénal et provoquait une sténose.

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FROM THE RADIUM CENTRE, COPENHAGEN (CHIEF: JENS NIELSEN, M. D.) AND THE OTOLARYNGOLOGIC SERVICE OF THE FINSEN INSTITUTE (CHIEF: OVE STRANDBERG, M. D.)

ROENTGEN TREATMENT IN CANCER OF THE LARYNX[1]

by

Jens Nielsen and *Ove Strandberg*

Part I. Indications and Results

Since 1931, when protracted fractional roentgen treatment after COUTARD's method was first taken up and practiced at the Radium Centre in Copenhagen, a quite considerable number of cases (about 600) of tumors in the upper air- and alimentary passages have been treated there in collaboration with the otolaryngologic service of the Finsen Institute. Among them are 63 cases of intralaryngeal cancer, which form the basis of the present communication.

The material is not selected. All patients with cancer of the larynx referred to us are included, and all the cases were primarily subjected to fractional roentgen treatment. The figures are thus absolute. We are personally conversant with all the cases and have collaborated in their treatment. Microscopic examination was made in all; except in a few that had a lethal issue, which makes their malignancy extremely probable.

Brief Review of the Ray Treatment in Cancer of the Larynx.

Though the application of roentgen- and radium rays to the treatment of laryngeal cancer was attempted as early as in 1903—4, it took long before reliable and comparatively safe methods of treatment could be worked out. Especially in the early twenties were there numerous reports of complications, often with lethal issue, in the form of perichondritis and cartilage necroses, which brought discredit on the ray treatment. It is true that LEDOUX and SLUYS, HARMER and FINZI, HALBERSTAEDTER

[1] Read at the XI. Congress of the Northern Association for Medical Radiology, in Stockholm June 14, 1941; submitted for publication July 17, 1941.

and SEIFFERT by making a window-shaped aperture in the thyreoid cartilage before introducing the needles had developed a technic of radium treatment that eliminated the risk of cartilage necrosis, and by that method obtained some lasting results; but it was suitable only for small cancers of the vocal cords limited to the central portion of one of these; in other words for the same forms and stages in which good functional and lasting results were obtained by laryngofissure. COUTARD had reported results of fractional roentgen treatment as early as in 1922, but it was not until after his presentation of a larger material at the 3rd international Congress of Radiology, in 1931, that his principles of treatment became the object of interest in wider circles. This material (1921—26) comprised chiefly inoperable or recurring cases of endolaryngeal cancer, and showed 5 years' freedom from symptoms in 16 of 77 cases (= 21 per cent). In his latest report, from 1939, which covers the period 1921—32, his material has increased to 142 cases, of which 39 (= 27 per cent) were symptom-free after 5 years or more. In 1939, SCHINZ (Zürich) published his results with fractional roentgen treatment *ad modum* Coutard, showing 5 years' freedom from symptoms in 6 out of 24 cases (= 25 per cent) and 3 years' freedom from symptoms in 9 out of 33 cases (= 27 per cent). These are the only existing reports of lasting results from Coutard treatment, so far; but many communications of primary results, of complications, or dealing with the technic of irradiation, etc., have in the last years appeared from various sides.

COUTARD himself has in several communications dealt with particular sites in the larynx, such as the false cords, with the technic of irradiation and the principles underlying the treatment; but he has not published any detailed report of the individual cases, and the same is the case with SCHINZ. On the part of the surgeons it is therefore with some justice objected against the Coutard treatment that we do not sufficiently know, yet, what forms and stages of cancer it is likely to cure and against which it is ineffective. Certain authors claim that it is applicable only to early, slightly extensive cases, and point out, besides, that COUTARD's results, according to his own statements, have varied so much from one year to another that the method can hardly be suitable for general use.

The discussion has been lively, and the interest in the Coutard treatment has in the last years been very great. The debate has centered especially about questions respecting the fields of indication for roentgen therapy and surgical treatment in cancer of the larynx. To the discussion of this subject, a weighty contribution was given at the international Congress of Otology, in 1936, by HAUTANT, who has collaborated with COUTARD at the Institut du Radium in Paris. In his opinion, the Coutard treatment is indicated, or promising of good effect, in such cases of carcinoma of the vocal cord in which the mobility of the cord is preserved, —

in other words in the same cases in which a minor surgical intervention (laryngofissure) gives good results. In these cases it therefore, according to HAUTANT, becomes a personal matter whether one prefers the Coutard treatment or operation. In cases where the vocal cord is immobilised he advises against Coutard treatment and recommends operation (hemilaryngectomy). In carcinomas of the vestibule of the larynx — especially of the false vocal cord — he recommends Coutard treatment, in preference to operation, because this localisation gives early glandular metastases, and because carcinomas in this site, as shown by COUTARD, usually are rather radiosensitive. On the other hand, he advises against Coutard treatment of subglottic carcinomas, which according to his experience are more frequent than carcinomas of the vocal cord itself. COUTARD himself has expressed the opinion that in cases where there is complete fixation of one side of the larynx it is at present impossible to obtain freedom from symptoms by irradiation; but otherwise he has not attempted to delimit the present fields of indications for surgical and radiologic therapy. FRENCKNER has set up a classification into various stages and given indications for their respective treatment by one of these therapies or the other; but there is nothing in his paper to show on what experiences and results of his own his statements are based, and he rather fails to consider the site of origin of the tumor. He recommends radium-bomb treatment (teleradium therapy) as at least equally efficacious as Coutard treatment; but with the exception of a few cases reported by EDLING there are no published records of lasting results obtained by this method. In cases where operation is performed, he recommends postoperative ray treatment.

It is possible that the time is not yet ripe for an exact delimitation of the respective fields of indications for surgical and radiologic treatment of cancer of the larynx; but as this question is a central issue in the discussion we shall in this communication make it a special point to bring forward such aspects of our material as may contribute to its better elucidation.

Principles and Technic of the Coutard Treatment.

This subject has already been dealt with in several publications from the Radium Centre, and need therefore be mentioned only briefly here. Our conception of the Coutard treatment as clinical irradiation experiments, and not as an established method of therapeutical procedure, is in conformity with the view of the inventor himself. The questions of tension, filter, distance, intensity, dosage, exposure time and reactions will not be discussed in detail. It should be remembered, though, that the treatment is a protracted fractional roentgen treatment extending,

with daily irradiations, over several weeks, and that the total dose is therefore considerable and often produces strong local, and sometimes general, reactions. In the years during which we have employed the method, we have varied the total treatment time for carcinomas of the larynx, within certain limits, from 3 to 8 weeks. At present we are inclined to prefer a treatment time of about 3—4 weeks for these cases. The total dose seems to lie around 5000 to 6000 — perhaps 7000 — *r* (measured in the air), depending on the size of the field and on the exposure time. The tumor dose must be at least 4500 to 5000 *r*. The size of the fields has been from 80 down to 50 square centimeters, sometimes less (35 sq. cm.).

We believe that the protraction is desirable as protection for the sound tissues. As a rule, it is necessary to produce the formation of pseudomembranes (epithelitis) in the larynx and dry or moist epidermitis. Perichondritis and necrosis of the cartilage we have never seen except in cases where the cancer had already invaded the cartilage before the treatment was instituted. Late cutaneous changes of any severity have never been observed. When the irradiation treatment succeeds, the functional results are extremely good. As a rule, the voice becomes natural and normal anatomical conditions are re-established. In the last years we have in severe cases, besides small initial doses, tried periodical treatment and multiple fractional — super-fractionated — treatment (up to 6 à 7 exposures in twenty-four hours). We have seen encouraging primary results of the procedure. In a great many instances it has been possible to deal with these cases throughout as ambulant cases. Sometimes, especially when the cancer has invaded the cartilage, it may be desirable or necessary to perform an inferior tracheotomy before beginning the treatment.

Biologic Conditions for the Irradiation.

Broadly speaking, what is determining for the radiologic treatment of larynx cancer — especially of its most frequent form, carcinoma of the vocal cord — is 1) that we have to do with a growth *which is not particularly radiosensitive*; i. e. it requires the application of a considerable ray energy to make the cancer recede; 2) *that there in the immediate neighborhood of the cancer are radiosensitive structures* (cartilaginous tissue); specially if an inflammatory or carcinomatous perichondritis has developed, which must be dealt with carefully if serious complications are to be avoided; 3) that we have to do with *a carcinoma of relatively small volume, which in most cases metastasises late and not very extensively, and for a greater part can be cured only by more or less mutilating surgical intervention*; and 4) that the cancer is *situated so comparatively superficial* that no serious technical difficulties oppose the application of a considerable ray dose.

Besides the technic employed, the following factors are of great significance for the result obtained by roentgen irradiation of a larynx cancer:

1) the histologic structure of the tumor;
2) its site (the point from which it arises);
3) its size and extent (the stage);
4) lymph node metastases;
5) perichondritis, involvement of the cartilage;
6) the general condition of the patient.

In every case of laryngeal cancer, these factors must be examined and considered as closely as possible before the choice is made between surgical and radiologic treatment, and on them depends in a great measure the technic of irradiation. Without thourough knowledge and experience, and without mastery in the application of the various methods of examination, one should not attempt the roentgen treatment of a larynx cancer. Just once in a while to treat some small, operable cancer of the larynx with roentgen must in the patient's interest be advised against as a hazardous undertaking; and as regards the inoperable forms and stages it is really only in appearance that one has a freer hand, because with insufficient experience one risks to lose the cases which may have become symptom-free with adequate irradiation.

1) *Histology.* — The great majority of carcinomas of the larynx are of the pavement cell type, with more or less complete phenomena of hornification. True epitheliomas of cutaneous type, with formation of actual onion bodies and with actual intracellular bridges are rather uncommon in the larynx, but parakeratosic formations frequently occur. From these, there are all transitions to more immature carcinoma-solidum forms. More important than a strict schematic classification is, however, that the histologist should be familiar with the different forms and in close touch with the clinic. He may then use either BRODER's classification of the stages, based on the differentiation of the cells, or the more finely differentiating, French classification (LACASSAGNE); or he may, as we have done at the suggestion of FRIDTJOF BANG, use a simplified nomenclature. All other things being equal, it may be expected that the less differentiated the carcinoma, the greater will the radiosensitivity be. Adenocarcinomas are uncommon, and so are sarcomas of the larynx.

2) The *site of origin* of the tumor and 3) its *extent.* — It is still being stated, almost as a dogma, that the true vocal cord is the most frequent site of origin of carcinoma of the larynx. The most recent researches seem to indicate, however, that this is not so absolutely the case as hitherto supposed. We have tried by direct laryngoscopy, roentgen examination in the form of lateral views of the soft tissues, and tomography, to as-

Fig. 1. Sites of the 63 cases of laryngeal Cancer from the Radium Centre.

A.	Vocal Cord	26	(? 33)*
B.	Subglottis	4	(? 12)
C.	Sinus of Morgagni	1	(? 3)
D.	Laryngeal Surface of Epiglottis	1	(? 2)
E.	Arytenoid Region	2	(? 3)
F.	Ventricular Band	9	(? 10)
		43	
	Too extensive to permit localisation of Site of Origin	20	
		63	63

* The figures in parentheses indicate the probable full number of cases in each group when those tumors are included whose site of origin could not be determined with absolute certainty.

certain as exactly as possible not only the extent of the tumor, but also its presumable site of origin. These methods of investigation can to a certain extent take the place of the pathoanatomic study of the operative specimens for which the surgical treatment affords opportunity. Further guidance is obtained from the tumor's reaction to the irradiation; especially from the fact that, as a rule, the portion of it which is the last to recede corresponds to its site of origin. According to their location, we have divided our cases into 3 groups: 1) *tumors arising from the true vocal cord*; 2) *tumors of the vestibule* (*the vestibular folds, the laryngeal surface of the epiglottis, the sinus of Morgagni*); and, 3) *the subglottic tumors*. As it will be seen from Fig. 1, the carcinomas arising from the true vocal cord constituted the majority, but not to such marked extent as stated from elsewhere; the number of carcinomas from the vestibule being relatively not inconsiderable. Tumors limited to the subglottis were not nearly as frequent, however, among our cases, as they are stated to be by HAUTANT.

As we know, the growth of *carcinomas of the true vocal cord* is relatively slow and remains for some time limited to the free border of the cord; and lymph node metastases do not arise until in the later stages. This accounts for the good results obtained by laryngofissure and excision in the early stages, and which, even in more advanced cases, can be obtained by laryngectomy or hemilaryngectomy, when suitable ones are selected. As long as the carcinoma has not invaded the muscle, and the mobility of the vocal cord is good, it reacts satisfactorily to a sufficiently strong roentgen treatment and is made to recede fairly easily, regardless of whether microscopy shows that there is a greater or lesser tendency to hornification phenomena. But when the tumor cells have invaded the muscle, which shows itself in a more or less reduced mobility of the vocal cord, the difficulty of successful roentgen treatment increases considerably. In a number of cases in which the fixation of the cord was less pronounced, we nevertheless obtained freedom from symptoms. In the

more advanced degrees of fixation such a result is seldomer obtained; endolaryngeal edemas occur, and it is difficult to make the tumor regress. If there is any considerable carcinomatous invasion of the cartilage, it will hardly be possible to obtain sterilisation by means of irradiation; because perichondritic lesions will occur, with edemas and sequestration of cartilage, which compel one to discontinue the treatment. Several cases of moderate extension from the true cord to the sinus of Morgagni and the inferior part of the false cord, or to the subglottis, we have succeeded in making recede completely, without complications, by irradiation. In cases where the arytenoid cartilage is involved it seems very difficult to obtain a favorable reaction. The cases most amenable to radiation therapy are absolutely those in which the mobility of the vocal cord is still entirely unimpaired, or nearly so. When that is the case, it does not matter if the tumor extends to greater or lesser portions of both cords, — a type which is not uncommon in our material, and for which laryngofissure must be considered as an unsatisfactory technic. Altogether it is our impression that in the cases where the fixation is not too absolute, and where there is no manifest involvement of cartilage, it may be justifiable to make a *test irradiation* in order to find out how the tumor reacts to this form of treatment. If it reacts, without local complications, during the first part of the irradiation, there is good hope that by continued treatment with full dose freedom from symptoms may be obtained.

Carcinomas of the false vocal cord are for the most part rather markedly radiosensitive. As hoarseness is not a pronounced early symptom of tumors in this site, they have, as a rule, reached a considerable extent by the time they come to treatment. They are often bilateral, and in many cases there are palpable lymph nodes in the neck. The tumors oftenest occur in the form of soft, papillomatous, protruding, exophytic masses, which, horseshoe-shaped, may fill the entire laryngeal vestibule. They are often composed of immature forms of squamous epithelium cells without tendency to hornification; sometimes they are more or less immature cylinder cell carcinomas. The lymph node metastases may attain a considerable size and are found chiefly corresponding to the superior, deep cervical lymph glands. They are seldom as fixed and inflamed as metastases from carcinomas of the vocal cord or the subglottis; and, like the primary tumor, they usually respond well to irradiation. The tumor does not invade the perichondrium and the cartilage until late; but the forms arising from the neighborhood of the stalk of the epiglottis have a tendency, already in an early stage, to grow through the epiglottis and invade the pre-epiglottic space.

In the *sinus of Morgagni*, the carcinomas seem to occur chiefly in two forms: either as papillomatous tumors prolapsing out through the

ventricle (our material contains a case of this kind) or as more diffuse infiltrations of the entire ventricle which may displace the false vocal cord upwards and towards the middle, so that it covers the true cord. In some cases, larger ulcerations may form. Though these carcinomas probably have a somewhat greater tendency than carcinomas of the false vocal cord to involve the cartilage, they seem to possess a not inconsiderable degree of radiosensitivity. As they are recognised later, and produce lymph node metastases earlier, than carcinomas of the vocal cord, they may, according to our experience, if the case is not too advanced, be treated by radiation therapy with some prospect of obtaining freedom from symptoms.

Carcinomas of the subglottis are prone to early extension to the perichondrium and invasion of the cartilage. Their route of spread is to a marked extent along the plane, both superiorly and inferiorly, often under the mucous membrane. But they do not spread as rapidly to the opposite side as the carcinomas of the false vocal cord. Lymph node metastases appear earlier than in the case of carcinomas of the vocal cord; often there will be a node on the mid-line of the anterior side of the neck, on the cricothyroid membrane. The diagnosis may be difficult if the inferior surface of the cord is involved and fixation of the latter in adduced position prevents inspection of the subglottis. Roentgen examination, especially tomography, may be very helpful in delimiting especially the inferior delimitation of the growth. This location of the tumor is hardly a very favorable one for radiation therapy, and in cases where the growth has not spread beyond the larynx, primary laryngectomy or hemilaryngectomy, without preliminary attempt at irradiation, should probably be considered.

3) The *late stages* of laryngeal carcinoma, where there besides extensive, infected, ulcerated, often bilateral infiltrates in the larynx are destruction of cartilage and extension beyond the boundaries of the larynx and to the soft tissues of the neck, do not seem to be amenable to radiation therapy except in mild doses as a palliative measure.

4) *Lymph node metastases.* — As already said, irradiation with roentgen may have a good effect on these, even if the nodes have reached a rather considerable size, provided the primary tumor has its site of origin in the false cords. Regression of metastases from carcinomas of the true cord or the subglottis we have seen only in the case of nodes of lesser volume, up to the size of a hazelnut.

5) *Involvement of cartilage.* — While the sound cartilage supports irradiation with the doses employed without any resulting immediate or late lesions, cancerous infiltration, with the usually accompanying inflammatory phenomena, will, as mentioned above, result in sequestration of

the cartilage areas involved when irradiation is attempted, and will thus, as a rule, make it necessary to interrupt the treatment.

6) *The general condition.* — While the general condition of the patient will in many cases contraindicate surgical operations of any magnitude, the same is not to any considerable extent the case as regards radiologic therapy. The risks in that respect depend in a great measure on the volume of tissue transirradiated (the size of the fields); and as, in treating endolaryngeal carcinomas, relatively small fields may be used, no marked effect on the general condition is observed. We have, without complications ensuing, treated cases of laryngeal carcinoma complicated with heart disease, pulmonary tuberculosis and diabetes mellitus without any of these concomitant diseases getting aggravated as result of the treatment, and without it having been necessary to interrupt the latter or to any extent modify the procedure on account of these affections. Nor has the age factor in any case contraindicated irradiation. Some of our patients have been over 80 years old and have supported the treatment without any difficulty worth considering.

The Results obtained and Discussion of these, especially with a view to Comparison between surgical and radiologic Treatment of laryngeal Cancer and a possible Delimitation of the respective Fields of Indication for the two Methods.

Our material is too small to form the basis for any actual statistics of treatment, but in Tables I—II will be found some numerical expressions for the results, and Fig. 2 illustrates the classification, according to the stage of the disease, which we have adopted in order to make it possible to compare our results with those obtained by surgery.

Our requirements for the definition of the stages has been as follows:

Stage I (comprising cases which may be considered as operable by laryngofissure + extirpation of the tumor): that the carcinoma be localised to the anterior two-thirds of a single vocal cord, reaching, and perhaps involving, the anterior commissure, but not extending beyond the latter; posteriorly not reaching behind the vocal process; free mobility of the cord.

Stage II (comprising cases which require a special technic of laryngofissure and excision): that the carcinoma involve, besides the anterior commissure, a greater or lesser portion of the anterior part of both the true vocal cords; and that the mobility of the latter is free or only slightly impaired.

Table I

Results of protracted fractional Roentgen Treatment in 63 Cases of laryngeal Cancer

Alive, symptom-free	Entire Material (63)	Stage I (6)	Stage II (8)	Stage III (21)	Stage IV (28)
5 years and over . . .	*5 : 23 (= 22 per cent)	1 : 1	2 : 2	1 : 5 (= 20 per cent)	1 : 15 (= 7 per cent)
3 years and over . . .	14 : 42 (= 33 per cent)	3 : 3	3 : 3	4 : 13 (= 31 per cent)	4 : 23 (= 15 per cent)
1 year and over . . .	25 : 54 (= 46 per cent)	5 : 5 (= 100 per cent)	5 : 5 (= 100 per cent)	10 : 19 (= 53 per cent)	5 : 25 (= 20 per cent)
Primarily symptom-free	31 : 63 (= 49 per cent)	6 : 6 (= 100 per cent)	8 : 8 (= 100 per cent)	12 : 21 (= 57 per cent)	5 : 28 (= 18 per cent)

* Two other patients are alive, symptom-free, over 5 years after the conclusion of the treatment, but are here considered as belonging to the »not symptom-free» group, because recurrences occurred, which only have ceased to give symptoms after surgical operation. In one of these cases (belonging to Stage III) the patient had been symptom-free for $4^1/_2$ years after the radiation treatment, when a local recurrence occurred, for which laryngectomy was performed. Since then, he has been symptom-free for 1 year. In the other case (belonging to Stage IV) there still, after the radiation treatment, remained a small residual tumor in one of the false vocal cords, wherefore hemilaryngectomy was performed 2 months later. The patient is alive, symptom-free, 5 years after this operation.

Table II

Results of protracted fractional Roentgen Treatment in 63 Cases of laryngeal Cancer

Alive, symptom-free	Operable	Inoperable
5 years and over	3 of 3	3 of 20 (= 15 per cent)
3 years and over	6 of 10 (= 60 per cent)	8 of 32 (= 25 per cent)
1 year and over	13 of 16 (= 81 per cent)	12 of 38 (= 32 per cent)
Primarily symptom-free	16 of 20 (= 80 per cent)	15 of 43 (= 36 per cent)

Of the patients in Stage I, 2 were poor objects for surgical therapy (1 aged 74, 1 with pulmonary tuberculosis).
» » » » » II, 3 were poor objects for surgical therapy (1 aged 73, 1 aged 79, 1 with myocardial degeneration).
» » » » » III, 10 were biologically inoperable on account of age (from 70 to 89 years).
All patients » » IV, were considered to be technically or (and) biologically inoperable.

Thus, only 20 cases (one-third of the material) could be considered as really operable, while 43 (two-thirds of the material) were inoperable.

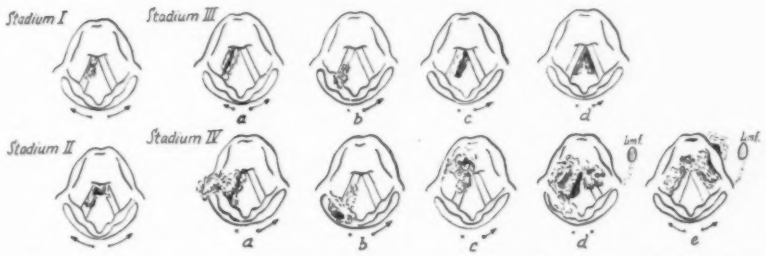

Fig. 2. Classification of laryngeal Cancers according to the Stage of the Disease.

Stage I: The tumor limited to the anterior two-thirds of one of the true vocal cords. The mobility of the cord unimpaired. Perhaps invasion of the anterior commissure, but no farther extension.

Surgical treatment: Laryngofissure and extirpation of the cord. (1:1 — 3:3 — 5:5 — 6:6)*.

Stage II: The tumor involves the anterior commissure and (perhaps) a greater or lesser part of the anterior two-thirds of the true vocal cord. The mobility of the cord unimpaired.

Surgical treatment: Laryngofissure, with partial removal of cartilage. (2:2 — 3:3 — 5:5 — 8:8)*.

Stage III: Extension of the tumor beyond the vocal cord. The cord more or less fixed. Unilateral or bilateral. No lymph nodes.

Surgical treatment: Laryngectomy (subsidiarily hemilaryngectomy).

a. Invasion of the vocal muscle, perhaps of the sinus of Morgagni and the false vocal cord (perhaps of the subglottis) (10)**.
b. Extension to the anterior side of the arytenoid region (2)**.
c. » » » subglottis (7)**.
d. Tumor arisen in the subglottis (2)**.

(1:5 — 4:13 — 10:19 — 12:21)*.

Stage IV: Extension of the tumor beyond the larynx. Frequently lymph nodes. Inoperable.

a. Invasion of the pharyngoepiglottic fold.
b. Infiltration of the arytenoid region.
c. » » » epiglottis.
d. Diffuse tumor growth in the interior of the larynx; destruction of cartilage As a rule lymph nodes.
e. Tumor arising from the false vocal cord (or from the laryngeal surface of the epiglottis). Frequently extension through to the pre-epiglottic space. As a rule lymph nodes.

(1:15 — 4:23 — 5:25 — 5:28)*.

* The figures refer to our number of cures and cases with observation times: 5 years, 3 years, 1 year and primarily symptom-free.

** The figures indicate our number of cases of the type in question.

Stage III (cases operable by laryngectomy, subsidiarily by hemilaryngectomy): that the carcinoma has invaded the muscles of the vocal cord and caused more or less pronounced fixation of the latter, or extends backwards around the articular process, perhaps involving the anterior side of the arytenoid region. Possibly some extension to the subglottis, or to the sinus of Morgagni and the false vocal cord. No demonstrable lymph node metastases. — As Stage III we have classified also subglottic carcinomas that have not yet produced lymph node metastases.

Stage IV: that there be extensive invasion of the carcinoma into the interior of the larynx, perhaps with growth through the arytenoid region or the epiglottis, or invasion of the pharyngoepiglottic ligament or other involvement of the hypopharynx (that the carcinoma has spread beyond the limits of the larynx). All cases with metastases to the lymph nodes are classified as Stage IV. In the extreme cases there is infiltration of the tumor into the soft tissues of the neck, necroses and ulcerations, obstruction of the larynx and cartilage necrosis. As Stage IV are also rated carcinomas of the vestibule, on account of their tendency to metastasise, and extensive subglottic tumors to which metastases and infiltrative growth into the surroundings seem to contraindicate surgical approach.

The case histories given at the end of this paper will serve to illustrate and further explain the principles of this classification.

As regards the biologic operability, as opposed to the technical, we have considered cases in which the patient was over 70 years old as biologically inoperable, as well as the cases presenting marked general or special complications such as myocardial degeneration, diabetes mellitus or pulmonary tuberculosis.

A classification like the above will, of course, always to a considerable extent be based on subjective estimate. Where there was doubt, we have usually chosen to place the case in a prognostically more favorable class, rather than taking a too pessimistic view of its operability. Study of the literature leaves one strongly convinced, however, that, ceteris paribus, the attainment of good operative results, whether by laryngectomy or by laryngofissure, depends in an immense degree on the selection of suitable cases, and that it will not do to draw the limits for operability too widely, if early recurrences are to be avoided.

Stage I comprises in our material 6 cases, all verified by microscopy. All the patients became primarily free of symptoms and remain so today. The voice is in all cases completely clear and natural. There have been no disturbing signs from the neck at any time. The skin of the neck within the fields of irradiation shows hardly any trace of damage. The treatment could be carried through without difficulty, and without either

general or local complications, because small fields could be used. The observation time for the different patients are as follows: one survives after $6^1/_2$ years, one after $3^1/_2$, one after 3, two after 2, one after 1 and one after 6 months. One patient, who was 74 years old at the time of treatment, died, free of symptoms, from old age, $3^1/_2$ years after being treated.

Stage II comprises 8 cases, all verified by microscopy. They all became primarily free from symptoms and have remained so since, with natural voice and without any alterations of either the skin, the soft tissues or the laryngeal cartilage following the irradiation. Also in these cases small fields were used, and the treatment was tolerated well in all cases except in one complicated by the co-existence of severe myocarditis, but where we nevertheless succeeded in carrying it through. This patient is now symptom-free 6 years after the treatment. The observation times are $7^1/_2$, 6, 3, 1 and 1 years; 9, 8 and 6 months.

Stage III. In these more advanced cases there is a more or less marked invasion of the cancer into the muscles of the vocal cord, with reduced mobility or complete fixation of the cord. In some cases the tumor had probably reached the perichondrium and had perhaps invaded the cartilage itself; in others it had extended to the subglottic space, where it spread and rapidly invaded the cartilage; or it had arisen there and attained some extension. In some cases the site of origin was the fortunately more uncommon in the posterior part of the true cord, with extension posteriorly and invasion of the articular process and the arytenoid cartilage. In many cases the sinus Morgagni and the false vocal cord were involved. There has been some difference of opinion about the significance of the fixation of the vocal cord as a clinical sign; but there can be no doubt that even a slight reduction of its mobility, beyond the merely mechanical that may be due to the size of the tumor, is of great importance for the determination of the stage of the disease, and thus for the choice of procedure and for the prognosis. This applies both to the surgical and the radiologic treatment.

Though far from denying that fixation of the vocal cord and extension of the cancer to the subglottis, or its origin in that site, must be considered as a serious symptom as far as the prognosis is concerned, we nevertheless from our experience believe ourselves justified in concluding that these factors do not always and so unconditionally aggravate the prognosis for Coutard treatment, or must be so determining for the choice of therapy, as maintained by FRENCKNER and some other authors. Our impression, based on our clinical experiences, is that in some cases of this type there is a possibility of obtaining lasting regression of the tumor by irradiation, and that it may therefore be justifiable to institute

a test radiological treatment, under most careful control of the carcinoma's and the mucosa's reaction to the irradiation, in order to find out if the case should be one of those in which the fixation soon gives way and the treatment can be carried through without complications such as edemas or necroses; and where there, consequently, is a chance not only of saving the patient's life, but also his larynx and its functions. Only greater experience with the irradiation will make it possible to say beforehand which of these cases must *a priori* be considered outside the domain of radiation therapy and should go directly to laryngectomy. The consideration for the possibility that surgical operation may be necessary later has in our opinion been considerably exaggerated. Among our material there are 2 cases which were successfully and without much difficulty treated operatively, by laryngectomy or hemilaryngectomy, respectively some months and $4^1/_2$ years after fully carried out Coutard treatment.

Experience so far seems definitely to indicate that the Coutard treatment may, on account of its good functional results, to a great extent, if not altogether, take the place of surgery in those cases of cancer of the vocal cord where the mobility of the cord is preserved. It seems to be comparatively easy and safe to make cancers of this type recede by means of a rather simple irradiation which no longer presents any great problems. It is to the cases where there is fixation of the vocal cord, and to the subglottic carcinomas, that the roentgen therapy must particularly direct its attention, and in respect to which it must try to make advance. To that end, close co-operation between the surgeon and the radiologist should be valuable, not only for the immediate practical results, but also for continued advances in the irradiation technic and increasingly better delimitation of the respective fields of indication for surgical and radiologic therapy. For our part we have no objection to all technically and operable carcinomas of the vocal cord where the cord is immobilised being subjected to laryngectomy or hemilaryngectomy, provided that there is a good laryngologic surgeon to perform the operation. Radiotherapy must in that case, for the time being, confine its work to the biologically inoperable cases and make its experiences with these. In practice, and especially if no sufficially qualified surgical assistance is available, we think that it may be justified to try a test irradiation. If it during the course of this is found that the tumor regresses and the vocal cord becomes less fixed, and that neither necrosis, infections or local edemas develop in the larynx, the irradiation may be continued to full dose. But if it is seen that the case responds unfavorably, even to small single doses, that there soon come local edemas of the mucosa, and the fixation does not relax, the treatment must be discontinued and the case referred to the surgeon for laryngectomy. Careful daily laryngoscopy is necessary

in these cases, and to attempt irradiation unless one has a large clinical experience must be adviced against. Sometimes it may be possible, perhaps by the use of small »preparatory» doses, to get a good way along with the treatment without any complications ensuing. In such cases the decision of whether it should be attempted to carry it through to the end, or whether it should be relinquished in favor of laryngectomy at a later time may be made when about two-thirds of the total dose have been given.

What we have said here must, of course, only be taken as immediate tentative lines of direction for the treatment. The reason why we have gone into so great detail on the subject is that, in our opinion, the choice between radiation treatment and laryngectomy in this stage is difficult. If all the cases are referred for laryngectomy, there is no doubt that some operations will be performed which might have been avoided; if they are all given over to radiation treatment there may be a risk of depriving the patient of the chance of preserving his life at the cost of his larynx. We believe that in the test irradiation spoken of we have a possibility of distinguishing between the two types of procedure without exposing the patient to any risk. Only increasing experience will show whether this road is practicable. So far, all our patients, also those in Stage III, have primarily been subjected to radiation treatment. This has been done for several reasons. Not only has it been desirable to gain experience, but several of the cases have been referred to us expressly in order to avoid operation, and other patients have themselves refused to be operated upon.

Experiences seem to show that in a certain number of cases it is not, at present, possible to give up laryngectomy if a cure is to be obtained; even if the number of such cases in our opinion is not very great and there hardly, so far as Denmark is concerned, can be a question of any very large material. We do not know for certain how many fresh cases of laryngeal cancer there are in the course of a year in the whole of the country; still, we have some basis for an estimate in the fact that, according to the statistics of the National Health Service, the yearly number of deaths from that cause is between 20 and 30; that is to say about 0.5 per cent of all cancer deaths. (Statistics, postmortem reports and similar sources from other countries show similar figures, varying from 0.2 to 1.1 per cent. St. Clair Thomson gives the ratio as 1.8 per cent, but this includes the extrinsic carcinomas). The yearly number in Denmark can hardly be supposed to be more than somewhere between 30 and 100, — perhaps 50. If 10 to 20 per cent of these are operable by laryngofissure and a similar proportion amenable to more radical surgical procedures, this will mean, in figures, about 10 laryngofissures and about 10 laryngectomies per year. These, at any rate small, absolute figures — as an expression

for the rare occurrence of carcinomas in this site — must be borne in mind when the question of a centralisation of the surgical and radiologic treatments of laryngeal cancer in Denmark is deliberated. If the necessary experience and practice is to be acquired, maintained and further developed, the material is hardly large enough to justify more than one centre of treatment.

What, now, is the reason for this great increase in the difficulty of treating a laryngeal carcinoma radiologically when the vocal cord is fixed? — In most cases it is undoubtedly invasion of the perichondrium and cartilage. We know from cancer in other sites, especially from cancers of the external ear, that invasion of the cartilage is a serious complication, both because it injures the latter and thus deprives it of its power to resist the radiation treatment and causes it to respond by necrosis and perichondritis, but undoubtedly also because the cancer cells in the new soil react less readily to the irradiation. In some cases invasion of the muscles alone is probably sufficient to explain the carcinoma's increasing resistance to the rays, because the cancer cells also in this soil lose some of their radiosensitivity. We have tried if it was possible from our cases to pick out certain forms or types among the different fixations, or degrees of fixation, of which it might be expected that they would respond more favorably to irradiation, but beyond what has already been said about the localisation in the larynx and the histologic structure this is hardly possible at present. It is our impression that the cases in which there is tumor invasion around the vocal process and into the anterior side of the arytenoid region are not favorable objects for radiation treatment, and that extensive cases with complete immobility of one side of the larynx — as also pointed out by COUTARD — cannot be expected, either, to respond well to irradiation; whereas the cases in which the mobility is impaired only to a lesser extent react more favorably, even if there is some involvement of the sinus of Morgagni or the subglottis (see the case histories at the end of this paper). Cases in which there is indubitable invasion of the thyroid cartilage cannot be expected to respond favorably to irradiation. Conversely, we have had instances where a tumor which, owing to invasion of the cartilage, did not tolerate irradiation responded well to radiologic treatment of an extensive recurrence following laryngectomy. Also extensive subglottic carcinomas are evidently, as HAUTANT has pointed out, unfavorable objects for radiation therapy. In a case of polymorphocellular, myogenic sarcoma of the subglottis (the only case of laryngeal sarcoma on our material), irradiation made the tumor recede completely, with no local recurrences, but the patient eventually died of metastases to the lung.

Our results in *Stage III*, which comprises 21 cases, are as follows One patient, aged 72, lived symptom-free for over 5 years and died

without recurrence, of an unrelated disease. One remained symptom-free for $4^1/_2$ years, after which time a recurrence developed in the subglottis; after laryngectomy he has now been symptom-free for 1 year. One survives, symptom-free, after $3^1/_2$ years; one symptom-free, after $2^1/_2$ years; one, symptom-free, after 1 year; one, symptom-free, after 1 year. One patient died after 2 years, during which there had been no local recurrence; one, aged 89, also without recurrence, from cardioplegia, after 1 year. Two are alive, free from symptoms after 6 months.

Of the 21 cases, about one-half (11) were operable by laryngectomy, while 10 were inoperable owing to age or other complications. If we consider only the 11 operable ones, the results of the treatment are:

free from symptoms for 5 years and over	0 of 1
» » » » 3 » » »	3 » 6
» » » » 1 » » »	8 » 10
primarily symptom-free	10 » 11.

The results in *Stage IV*, which comprises 28 inoperable cases, are, of course, modest. In the terminal stages of carcinomas arising from the true vocal cord and the subglottis it cannot be expected to obtain freedom from symptoms when there is invasion of the soft tissues of the neck, severe lesions of the cartilage and metastases to the lymph nodes. With carcinomas that could be localised to the false vocal cord, and in which there were, as a rule, metastases to the lymph nodes, the results were better:

free from symptoms for 5 years and over	0 of 3
» » » » 3 » » »	3 » 8
primarily symptom-free	5 » 9.

Besides the 3 of 8 patients who survive symptom-free after more than 3 years (see the case histories), one of these 8, on whom hemilaryngectomy was performed for a small residual tumor in one of the false vocal cords 2 months after the termination of the roentgen treatment, survives after more than 5 years. As already said, we can therefore subscribe to the views of COUTARD and HAUTANT respecting carcinomas of the false vocal cord as favorable objects for radiologic therapy.

A woman, aged 73, with a papillomatous carcinoma of the sinus of Morgagni and unilateral metastasis to the lymph nodes is still alive, symptomfree and with clear voice, 5 years after the treatment. In 2 cases the carcinoma seemed to have arisen from the anterior side of the arytenoid region and had invaded the false vocal cord. In one of these cases the treatment was interrupted owing to poor response to the irradiation and the patient referred to the laryngologic service for laryngectomy. A large local recurrence a few months after the operation receded completely after roentgen treatment. The patient is still alive, with no local recur-

rence, 4½ years after the operation, but there are now metastases to the lung.

It is not possible to make a direct comparison between our results as a whole and surgical results with a corresponding material, because it must be remembered that our material is in no way selected, whereas any surgical material is in itself a selected one. In order to arrive at some sort of comparison nevertheless, we have in Table II tabulated our cases under two headings: *operable* (*by laryngofissure or laryngectomy*) and *technically or biologically inoperable*. In this connexion we also reproduce, in Table III, some figures respecting surgical results by laryngofissure, hemilaryngectomy and laryngectomy from the collected statistics from the literature by WEBER (1928).

Table III

Surgical treatment	Author	Number of cases	Operative mortality	Symptom-free (3 years)
Laryngofissure	WEBER (20 Surgeons)	432	32 (7 per cent)	126 (29 per cent)
»	» (early stages only)	165	6 (4 »)	134 (81 »)
»	ST. CLAIR THOMSON	70	3 (4 »)	32 (46 »)
»	SCHMIEGELOW	33	5 (15 »)	18 (54 »)
»	GLUECK and SOERENSEN	126	6 (5 »)	109[1] (87 »)
Hemilaryngectomy	WEBER (20 Surgeons)	137	22 (16 »)	14 (10 »)
Laryngectomy	WEBER (20 Surgeons):			
	total cases	605	58 (10 »)	147 (24 »)
	strictly endolaryngeal	104		(38 »)
	with lymphnode metas.	289		(17 »)
»	MC KENTY (small endolaryngeal)	64	2 (3.1 »)	32 (50 »)
»	TAPIA	106	5 (4.7 »)	24 (23 »)

The operative results will, of course, depend immensely on the selection of cases made. This is evident from the personal statistics. When laryngofissure is attempted in cases where the carcinoma has extended to the anterior commissure or has penetrated into the depth of the cord, a cure percentage of 80 per cent, which it is possible to obtain only in the early stages of tumors limited to the medial one-third of the vocal cord, cannot be counted on, and the percentage will drop to about 30. If laryngectomy, as done by MCKENTY, is performed even for early intralaryngeal carcinomas, freedom from symptoms may, with the use of a satisfactory operative technic, be obtained in as much as 50 per cent of cases, but if also more advanced cases are included the percentage falls to 25. Hemilaryngectomy is, according to the German authors, a tech-

[1] A small number of cases with too short observation time are included.

nically more difficult operation than total extirpation of the larynx, and the lasting results more uncertain, and is therefore advised against by most of them. In France, where there, from humane considerations, has been some hesitation about employing the mutilating total laryngectomy, hemilaryngectomy still has a foothold though, and is recommended by HAUTANT, among others.

It lies outside the limits we have set ourselves for the present communication to enter upon a discussion of the degree and extent of the mutilation resulting from laryngectomy. Some authors go so far as to entirely oppose this procedure on account of its seriously disabling results for the patient. Others are hesitating or vacillating in their judgment. But most surgeons think that the development of a pharyngeal or esophageal speaking-voice, which is possible in most cases, not only reconciles the patient to the loss of his natural voice and respiration per viam naturalem, but as a rule does not make him so much of an invalid that he is debarred, henceforth, from filling his place in the community. None the less it is certain that it would be a great step in advance if the radiation therapy, with its good functional results and its preservation of the natural respiratory tract could take the place of and render superfluous the surgical treatment of laryngeal carcinomas, especially those forms that now demand laryngectomy. This cannot be said to be possible yet as regards all cases, but the results of the protracted fractional roentgen treatment after COUTARD's principles are already now so promising that they encourage not only to continued efforts, but in a not inconsiderable number of cases to consider the possibilites of that therapy in preference to surgical procedures.

We have not spoken of the combination of surgical and radiologic therapy, because in our opinion it does not offer essential advantages, whereas there is a certain risk that neither of the two treatments may be thoroughly carried through to the end. A choice should be made: *either* irradiation *or* surgery. Nor can we see that anything is gained by postoperative radiologic treatment (as a rule in moderate doses) after a presumably radical surgical operation. This form of irradiation is based on out-of-date or unconfirmed theories about the effect of irradiation in cancer. If the surgical operation has been radical, prophylactic irradiation is in our opinion superfluous; if it has not, the postoperative irradiation must be given as an actual curative treatment with full dose.

Attempt to define the respective Indications for radiologic and surgical Therapy in Cancer of the Larynx.

Stage I: *Laryngofissure* or *Coutard treatment* may be chosen. If the cancer is not very small and localised to the middle one-third of

the vocal cord, roentgen treatment is probably to be preferred, not only on account of the good functional result (natural speaking-voice), but also because with this therapy a larger extent of the cancer does not seem to matter so much, as long as the mobility of the cord is unimpaired.

Stage II: *Coutard treatment*, *extended laryngofissure* or *laryngectomy* are the procedures of which there may be question. Laryngectomy must be advised against as too radical an operation in this stage. Extended laryngofissure can hardly be regarded as an absolutely safe operation. Coutard treatment must be considered as the most suitable therapy, because it seems to give just as good functional and lasting results as in Stage I.

Stage III: The choice lies between *laryngectomy* (possibly *hemilaryngectomy*) and *Coutard treatment*. The last named therapy seems to be suitable for carcinomas of the false vocal cord, which metastasise early and are rather radiosensitive. As HAUTANT expresses it: this is a »good» radiologic cancer, a poor surgical one. In cases of fixed carcinomas of the vocal cord laryngectomy may be chosen if the immobility is complete; if it is less pronounced a test irradiation may be tried, and the choice between surgical and radiologic treatment be made on the basis of this. In cases of more extensive subglottic carcinomas laryngectomy is to be preferred; as HAUTANT says, this is a »good» surgical cancer, but a poor radiologic one. Carcinomas of the sinus of Morgagni seem hold an intermediate place, between the carcinomas of cord and those of the subglottis. As they metastasise rather early, a tentative irradiation may be tried.

Stage IV: In these cases *irradiation* is the only therapy of which there can be question (besides tracheotomy as a palliative). Carcinomas arising from the false vocal cord are the only ones in which it can be expected that a curative irradiation may be carried through with prospect of freedom from symptoms. In the other cases the greatest relief will probably at the present time be obtained by confining the radiation treatment to small palliative doses.

(To be continued in next number).

PROCEEDINGS

OF

THE NORTHERN ASSOCIATION FOR MEDICAL RADIOLOGY

(– NORDISK FÖRENING FÖR MEDICINSK RADIOLOGI –)

AN ACCOUNT OF THE ELEVENTH MEETING OF THE ASSOCIATION

HELD IN STOCKHOLM

JUNE 14th—15th 1941

Edited by

Carl Sandström, Secretary-General.

ORGANISING COMMITTEE:

GÖSTA FORSSELL, *President.*
CARL SANDSTRÖM, *Secretary-General.*
NILS WESTERMARK, *Hon. Treasurer.*
HANS V. SAHLSTEDT, *Secretary.*
BO STENSTRÖM, ELIS BERVEN, LARS EDLING.
JAMES HEYMAN, ERIK LYSHOLM, ÅKE ÅKERLUND.

14—420088. *Acta Radiologica. Vol. XXIII.*

MINUTES OF THE 11th MEETING OF THE NORTHERN ASSOCIATION FOR MEDICAL RADIOLOGY

held in Stockholm June 14th and 15th 1941.

Opening Session, June 14th 1941.

§ 1.

The President, Prof. GÖSTA FORSSELL, declared the Meeting opened.

§ 2.

At the suggestion of the Council it was decided not to nominate any Honorary Presidents or special Secretaries for this meeting.

§ 3.

At the unanimous suggestion of the Council it was resolved, on account of the increased cost of printing, no longer to publish the transactions of the Society in Nordisk Medicin but only in English in Acta Radiologica. The papers would be published in German, English or French in Acta Radiologica as original articles and in the original language in any of the Northern journals of Nordisk Medicin. The reports on the proceedings in Acta Radiologica should only include titles of papers and the place of publication besides contributions to discussions.

§ 4.

The Auditor's report was read and the Treasurer-General discharged from liability.

§ 5.

Professor LARS EDLING was appointed to check and sign the minutes of the day, together with the President.

§ 6.

Since there was no further business on the program, the Society immediately passed on to the scientific proceedings.

The minutes kept by:
CARL SANDSTRÖM,
Sec.-Gen.

The minutes checked and signed by:
GÖSTA FORSSELL.
LARS EDLING.

Closing Session, June 15th 1941.

§ 1.

The President declared the session opened.

§ 2.

At the suggestion of the Council it was unanimously decided to hold the next meeting in Lund, if possible, in the first half of June 1942.

§ 3.

At the suggestion of the Council it was resolved not to set down any subjects for discussion for the next meeting and that the meeting should be held under the simplest possible forms.

§ 4.

As President for the next period of office was unanimously elected Professor LARS EDLING, Lund.

§ 5.

As Secretary-General for the next period of office was elected Dr. CARL SANDSTRÖM and as Honorary Treasurer Dr. NILS WESTERMARK.

§ 6.

As members of the Council were elected: P. FLEMMING-MØLLER, CARL KREBS (Denmark), CARL WEGELIUS, S. MUSTAKALLIO (Finland), T. DALE, R. BULL ENGELSTAD (Norway), ELIS BERVEN, HANS HELLMER, ÅKE ÅKERLUND (Sweden).

§ 7.

As Deputy Members of the Council were elected: JENS NIELSEN (Denmark), E. M. TAMMIA (Finland), H. REITAN (Norway), ERIK LYSHOLM (Sweden).

§ 8.

As Auditors were elected: Dr. CHR. BAASTRUP and Mr. CARL O. EDEMAR and as Deputy Auditors: Dr. HUGO AHLBOM and Mr. C. B. SCHMIDT.

§ 9.

Prof. ÅKE ÅKERLUND was appointed, together with the President, to check and sign the minutes of the day.

§ 10.

On behalf of all the delegates Dr. P. FLEMMING-MØLLER expressed his thanks to the President for the excellent way in which he had organised and led this scientifically so fruitful meeting.

§ 11.

The President declared the Congress closed.

The minutes kept by:
CARL SANDSTRÖM.
Sec.-Gen.

The minutes checked and signed by:
GÖSTA FORSSELL.
ÅKE ÅKERLUND.

The President, Professor Gösta Forssell,

in opening the Meeting, delivered the following address:

Ladies and Gentlemen,

I extend to you the most cordial welcome to Stockholm and to the eleventh Meeting of the Northern Association for Medical Radiology.

During the year 1940 it was for well-known reasons impossible for us, in accordance with resolutions adopted, to meet in Stockholm. It is therefore all the more agreeable to us all that the Association is able to hold its Meeting here. We see in this a beginning for a brightening in the World, a fresh evidence of the strength of spiritual and intellectual ties, and a sign of the vital force of the thought of Northern union and unity.

Since our last Meeting three of the *Association's Honorary Members* have passed away.

SEVERIN HEYERDAHL, who wielded the gavel when our Association was founded, and at our last Meeting was acclaimed as our paternal friend and leader, passed away on the 26th June, 1940, in his seventieth year.

We shall remember him as a pioneer and loyal champion of the science of radiology in Norway and the Northern Countries; as the founder of radiological instruction and tuition in Norway; as an ambitious and successful worker in the struggle against cancer; and, first and foremost, as the founder and organiser of the Norwegian Radium Hospital, which for future generations shall bear witness that SEVERIN HEYERDAHL thought highly of his science and his country, and devoted and sacrificed his best strength and power in their service.

CLAUDE REGAUD died at the end of December, 1940, at the age of seventy, after a long illness and mourning the loss of a son who died for his country. In pain and sorrow there passed thus away a man who had spent all his labourious life in the quest for new ways for medical science and the alleviation of suffering.

CLAUDE REGAUD's carreer was that of a scientist. His fundamental histological works on Spermatogenesis and Ovogenesis, and on the action of Radiation upon these biological processes brought him within the Sphere of Radiobiology and Radiotherapy. In 1911 he was appointed a teacher at the *Institut Pasteur* and chief of the Radiophysiological laboratory at *L'Institut du Radium de l'Université de Paris*. The Radiological Clinic established by him and his disciples in connection with this Institute, *La Fondation Curie*, has a world-wide reputation as a leading centre for research and instruction relating to cancer and its radiological treatment. REGAUD devoted himself altogether to his profession as a researcher, teacher and leader in the battle against cancer. His personality which was characterized by noble calm and seriousness has procured him friends and admirers throughout the world.

CHARLES THURSTAN HOLLAND died on the 16th January, 1941, at the age of 77, in Liverpool, where he carried out his whole life's work as »Honorary Radiologist» and Röntgen physician.

THURSTAN HOLLAND's scientific output is not on a large scale, but his practical work was of vast importance to Radiology. He never occupied any position as a university teacher but laboured nevertheless as an important pioneer by the example of his skilful and critical work and by his synoptical articles and lectures. No English Radiologist has in his native country and abroad enjoyed a greater reputation for experience, skill and good judgement than THURSTAN HOLLAND. He was awarded in England one after the other of those honours which can accrue to a man of his profession.

His greatest renown THURSTAN HOLLAND gained however as Chairman of the First International Radiological Congress in London, in 1925, where for the first time after the Great War 1914—1918 representatives for all civilized countries gathered for a scientific congress. He was a very highly esteemed member of later International Radiological Congresses. But he was prevented by illness and age to attend the last Congress in Chicago, and was greatly and sincerely missed by his large circle of friends. The older ones amongst us will remember with affection THURSTAN HOLLAND's original and humorous personality.

Two of the *Association's members*, both Finns, have passed away since the last Congress.

The roentgenologist at the County Hospital in Viborg, NURO ARNE BERNER M. D., passed away on the 25th August, 1940, at the age of 58. He succumbed to aplastic anaemia, a victim to the dangers and risks of his profession.

Titulary Professor OSKAR ARVID BOIJE M. D., died from lingering pneumonia on New Year's Day of this year, in Helsingfors, at the age of 72. He had a long and honourable carreer behind him as a medical practioner, scientist, university teacher and chief of the Gynecological Obstretic Hospital which he himself had established.

He was a lecturer at Helsingfors University between the years 1901—1928 and upheld on several occasions the Professorship in Obstetrics and Gynecology.

BOIJE advanced Radiology by establishing together with G. A. WETTERSTRAND, in 1914, a Radium- und Roentgen Institute at his hospital, one of the first institutions of its kind in Finland. He was also the first to take up in Finland radiological treatment in gynecology. From the inception of our Journal, in 1921, right up to 1939, BOIJE was a collaborant of Acta Radiologica.

He leaves behind him the memory of a conscientious and skilful teacher, a charming man and a good comrade.

Peace be to the memory of our departed colleagues!

Radiology is now with great strides approaching its second half-century, and the ranks of pioneers are growing thinner and thinner. Their great gifts to later generations and their devoted personal sacrifices on the Altar of Radiology lay it upon us to sacrifice, unselfishly, our own strength to and for the science which we have the fortune to serve.

The program of this small Meeting and the many scientists who have met here seem to me to spell good promises of the Northern Countries remaining a source of light for Radiology.

With this hope I declare this Eleventh Meeting of the Northern Association for Medical Radiology opened.

SCIENTIFIC TRANSACTIONS

Professor GUNNAR NYSTRÖM, Uppsala; Sweden: *Results in the surgical treatment of mammary cancer.*

Dr. HUGO AHLBOM, Stockholm; Sweden: *Statistic relating to the treatment of the mammary cancer from Radiumhemmet, Stockholm, 1921—1935.*

Dr. OLLE REUTERWALL, Stockholm; Sweden: *Heeling symptoms in irradiated cases of mammary cancer.*

Dr. R. BULL ENGELSTAD, Oslo; Norway: *Combined surgico-radiological treatment of cancer mammae.* (Cancelled, author prevented from attending.)

Discussion: J. CHYDENIUS, JENS NIELSEN, G. NYSTRÖM, FR. VON BERGEN, E. BERVEN, O. CHIEVITZ, SV. JUNGHAGEN, H. AHLBOM, GÖSTA FORSSELL.

Dr. J. J. CHYDENIUS, Helsingfors:

It is of great significance that a research worker of REUTERVALL's experience and reputation has made his voice heard on the question of histological healing phenomena in cancer treated by radiation. Although the enquiry in investigations of this nature perhaps seem as old as radiotherapy itself the problems connected with it are of great current interest.

In several places there has been a tendency to push aside the microscope as an antiquated instrument but this is not well-advised. The experimental and, biologically, apparently more accentuated research is still in need of histological methods. And the experiences gained with ovi and larvae, skin of salamander and tails of rats must finally find its application on true tumours and human material in order to bear any useful fruit.

Two years ago at the Gynecological Congress in Oslo I described some histo-pathological examinations of the healing process as obtained by radiotherapy of carcinoma of the neck of uterus after the Stockholm method.

Fortunate circumstances have brought into my hands a unique material of cases of cancer colli, first treated by radium and then by operation.

I draw attention here to the same points as REUTERVALL has spoken of to-day. »It must be considered established that the healing process is brought about as a result of radiation injuries arisen in the malignant cells which tolerate such damage worse than the surrounding tissues. But the importance of the general and local environment in a humoral as well as cellular respect must not be underrated. (p. 159—60). The cell changes observed are characteristic of a tissue treated by radiation. They are not, however, specific in this sense that similar cells were not to be found elsewhere. On the contrary changes of much about the same character also occur in such spontaneous degenerative processes that are more or less to be found in all carcinomata» (p. 191—192). Cure after treatment by radiation is thus an expression of a spontaneous tendency to healing. We have to do with a reversible process where the healing factors have once more gained the upper hand.

In the course of my investigations I have tried to compute in r-units the radiation doses that should be used to attain such a result. Although these investigations have already been published in Acta Obst. et Gyn, Scand. 1940 (Vol. XX, fasc. 2), I would like to show you a few pictures where the local reaction shows up particularly clearly (8 microphotoes),

Dr. JENS NIELSEN, Copenhagen:

When in Oslo two years ago the radiological treatment of cancer mammae was selected as the main therapeutic subject for this Congress I was hoping that the discussion to-day would help to clear up some of the questions which in this relation always are of extremely great importance for the surgeon as well as for the radiotherapeutist. I shall only mention some of the chief points.

The value of post- and preoperative radiation? To which should preference be given? Are there any definite clinical indications to show that as a prophylaxis against recurrences postoperative radiation in doses usually employed has any favourable effect? Technique and dosage in preoperative radiation? How long after radiation should the radical operation be performed? What results can be obtained by pure radiological treatment without operation and by local operation in addition to radiological treatment? Is sterilisation by roentgen of any value as an aid to treatment?

A study of the extensive literature concerned and the observation of my own cases have convinced me beyond doubt that time is not yet ripe for offering a clear answer to these questions. This is also evident from the introductory papers we have listened to to-day. Even Dr. AHLBOM's very large material which extends far back in the past offers no definite answer to any of the above questions.

My own material from the Copenhagen Radium Clinic is of more modest compass and can mainly serve to indicate along which lines we have taken up the treatment and and to help us to obtain a numerical estimation of the clinical impressions we have formed and which I will now very briefly put before you.

Table I gives our aggragate number of cases and I would like to say at the outset here that contrary to Dr. AHLBOM's figures our figures are absolute, in that no patients have been declined. Of particular interest is a comparative tabulation of those radiated preoperatively and those only treated by roentgen after the operation (Table I and II). It will be seen here that the 5-year results in these groups are 52 and 37 per cent respectively but that the figures are small.

As a whole year has passed since the above table was made up, I have now added also this year's cases and we then find that the relative results, even for these somewhat bigger figures, are very nearly as before.

	1931—35	1931—37	1931—40
Cancer mammae preop. radiation	68: 34 (50 %)	126: 71 (56 %)	252
» » operat. prophyl. rad. . .	125: 46 (37 %)	210: 97 (46 %)	339

Since both the operator and the surgical technique have a great bearing upon the permanency of the results, it should be noted that the two groups are in this respect scarcely directly comparable because those cases referred to postoperative radiation have been operated on by different surgeons while those preoperatively radiated were all operated on by one and the same surgeon, Prof. O. CHIEVITZ, whose surgical technique is very radical. It is quite likely therefore, at any rate possible, that the different results are in part or wholly due to this circumstance. On the other hand, preoperative radiation (Table III), affords such decided effect, as evident by clinical as well as histological examination, both on primary tumours and — though generally to a less extent — on metastatic glands, that I am going to continue with it on the belief that it holds possibilities of devitalisation of the tumorous tissue whereby the risk of propagation at a subsequent operation would be reduced (Table IV). Even if it may be said that it is always, as it were, the distant metastases that decide the ultimate fate of the patient, we can scarcely deny local recurrences and metastatic glands some importance as depots and starting points for such metastases.

The histological structure of a tumour is undoubtedly of decisive importance for the ultimate result of the radiation treatment but so far we are unable to say anything definitely, as to which are the histological forms that react favourably to irradiation. Preliminary clinical observation should here be our guide. Exploratory excision here undoubtedly affords us a valuable aid in the solution of these problems; by this method we are able, easily and surely, and with little traumatisation, to obtain a sufficient amount of tissue for histological examination before roentgen treatment is commenced.

I prefer to perform the radical operation about one month after termination of the roentgen treatment. The dry epidermitis arisen has then come to an end and there are no complications in the healing of the wound, at most a little suppuration of the sutures.

Should radiation be given after as well as before operation? I don't think so and I don't give it. I have always had very little belief in postoperative roentgen irradiation in small doses, the fundamental principles of which seem to me weak, based as they are on antiquated or non-verified opinions regarding some cancericide or local immunising effect.

I have gradually increased the doses in preoperative radiation, given tangentially on the breast over two fields, and I have now come up to a total dose of 2,100 r on each side, divided in single doses of 150 r, without noticing any complications so far either the operation or the healing of the wound is concerned. In addition the axilla is also irradiated and in the majority of cases — at any rate always when there are palpable glands in the axilla or the mammary growth is a large one — also the supra — and infraclavicular regions. It is only in such rare cases of small well movable mammary cancerous growths without any palpable axillary glands (well marked stage I, Steinthal) that one may permit oneself to discard the preoperative radiation and pass directly to radical operation.

As is also evident from Table I my experiences definitely point against advising roentgen therapy as the sole form of treatment for mammary tumours, as by such means complete sterilisation of the growth seem rare. I also advise against local excision of the tumour in conjunction with radiation treatment as a hazardous form of treatment.

Finally one must not forget drawing attention to the possibility we have in obtaining marked palliative effect, often of long standing, in progressive cases — particularly in the case of skeletal metastases — by roentgen treatment of ovaries before and partly during climacterics. It is really astounding improvements — even lasting up to several years — that can be observed here in perfectly hopeless cases. Nowadays I never fail to irradiate the ovaries in these cases but so far I have not taken upon myself the task of sterilising them by roentgen — in order to prevent metastases — as a routine treatment of younger women in conjunction with preoperative radiation treatment.

A particularly pronounced case of favourable distant effect of ovarian irradiation will now be briefly described.

Female, aged 42, underwent a radical operation for a large cancer growth in the left breast (microscopy: carcinoma solidum) in June 1938 and was given postoperative roentgen treatment in August, October and December 1938. Eight months after operation (Febr. 1939) she was found to have a cancerous growth in her right breast with glandular metastases in the right axilla. Microscopic examination of excised mammary specimen proved it to be a carcinoma solidum. (Probably metastatic cancer from the primary growth in the left breast.) Rightsided radical operation without radiation was undertaken in April 1939. Six months after the last operation (October 1939) widespread metastases were found in the spine (also collapse of 9th dorsal vertebra), in the skull, where there were several rounded rarefactions, the size of from peas to nuts, as also in a great many ribs with spontaneous fracture of the right 7th rib. There was also left abducens paresis (basal cerebral metastasis). No signs of metastasis of lung but there

Table I

Classification of the total number of treated cases of cancer mammae 1931—39 with 5-year results (1931—36) and 3-year results (1931—34).

	1931—34	1931—36	1931—39
C. mammae, preop. radiation	42 : 22 (52 %)	98 : 54 (55 %)	213
C. » , op. proph. rad.	96 : 35 (37 %)	167 : 76 (46 %)	293
C. » , op. of recurrence	113 : 2 (1.8 %)	177 : 5 (2.8 %)	299
C. » , inoperable	72 : 0	122 : 1 (0.8 %)	218
C. » , non-radical op.	—	—	23
C. » , operable, radiation tr.	25 : 2 (8 %)	51 : 9 (18 %)	77
Mb. Paget	2 : 1	5 : 4	12
Sarcoma mammae	1 : 1	2 : 1	7
Tumour mammae	3 : 3	6 : 4	16
Total	364 : 62 (17.2 %)	630 : 149 (23.7 %)	1,158
Total number ./. mammae op. rec.	247 : 60 (24.8 %)	453 : 144 (31.7 %)	

Table II

5-year results in the different stages of pre- and postoper. radiation 1931—1934.

Stage	Preoperative radiation	Postoperative radiation
Steinthal I	18 : 14 = 78 %	23 : 16 = 70 %
» II	21 : 10 = 48 %	33 : 6 = 18 %
» III	3 : 0 = —	—
Total	42 : 24 = 57 %	56 : 22 = 39 %
Total material	42 : 24[1] = 57 %	96 : 35[2] = 37 %

[1] 2 subsequently died after 6—7 years.
[2] 5 » » » » »

Table III

Immediate effect of preoperative radiation on primary tumour and axillary grands.

	0	+	++
Macroscopical	4	33	5
Histological	2	39	3

Table IV

Local recurrences, metastases of axillary and supraclavicular glands after pre- and postoperative radiation.

	Local recur.	Axillary glands	Supraclav. glands	Number of recurrences
Preop. rad	2 = 5 %	1 = 2 %	{5 (2) = 12 % (5 %)}	5 : 42 = 12 %
Postop. rad	24 = 25 %	19 = 20 %	27 = 28 %	36 : 96 = 38 %

were nodular growths in pelvis and abdomen. Well marked cachexia, Sahli 44 %. S. R. 15 mm.

Ovaries were treated by powerful roentgen radiation (5 × 200 r over each of 2 anterior fields and 4 posterior ditto of 150 cm²). Menopause followed. *No other roentgen treatment was given.* During treatment ascites developed, necessitating the evacuation of 6 litres of ascitic fluid. Repeated punctures had subsequently to be made but ascites gradually disappeared; her general condition improved and back pains abated, the abducens paresis disappeared. Twelve months later the patient was apparently well and quite fit to work. There were no local metastases or recurrences in the thorax or in the glandular regions. On roentgen examination of the skull the metastases earlier described in the theca cranii had entirely disappeared so that the appearance was now quite normal. Also the dorsal and lumbar spines where earlier a structure characteristic of metastasis had been found now showed almost normal condition; it was only in the uppermost lumbar and dorsal vertebrae that the structure still proved to be a little mottled. All metastases in ribs had disappeared and the bone tissue had been transformed; the spontaneous fracture earlier described had healed.

Another six months later (May 1941) patient had regained perfect health. Healthy complexion. General condition satisfactory. No clinical signs of recurrences or metastasis. (Not radiographed.)

Fr. von Bergen, Gothenburg:

It is only during the last few years that, here in Gothenburg, we have made full use of pre- and postoperative treatment of mammary cancer. My own material is too small to be submitted in this relation. Our mode of procedure has been as follows. Operation is carried out about 3 weeks after the preoperative treatment. In every case where there is clinically any doubt of the diagnosis being cancer the whole tumour is first extirpated and immediately sent for histological examination. The outcome of the examination is settled after half-an-hour; if this has revealed cancer or a pre-cancerous state operation is immediately performed. In the latter case the patient is not of course included in the cancer statistics.

I would also like to mention an observation we have made in some cases where excised small growths considered to be adenofibroma were ultimately found to be cancer. After preoperative treatment and operation the mammary tissue has in several cases shown the same appearance of invasion close to the scar as Prof. Reutervall has just been demonstrating. This shows that in exploratory extirpations, even if carefully carried out, not only lymph channels are opened up but strongly active tumorous tissue is also damaged with all the risks associated therewith.

Dr. Sven Junghagen, Umeå:

In the paper we have just been listening to I had expected to hear some data that might have been a help and support to us practising radiologists, particularly in what concerns dosage, its total magnitude and fractionation, as also the most suitable date for the surgical operation after termination of the radiation. For my own part I have preferred to give up to 3—4,000 r against the breast (tangentially) and against adjacent fossae in very protracted fractionation (roughly 100 r × 2); in relation to this a desquamating epithelitis has arisen which has, however, cleared up without much trouble to the patient. As to the date of operation I have followed the American authors who have suggested two months after termination of the treatment; this I have also found the most appropriate time as it seems to me that the most powerful regression of tumours takes place during the latter half of this »rest-period».

Dr. H. Ahlbom, Stockholm:

At Radiumhemmet we have for many years been giving 1,000—4,000 r over each field for 6—10 days (daily dose generally 350 r, one field only has been radiated each day).

In those cases where 1,400 r are given per field a dry epidermitis often arises which necessitates postponement of the operation till 5—6 weeks after termination of the radiation. In other cases operation is carried out 3—4 weeks after the roentgen treatment.

Prof. GÖSTA FORSSELL, Stockholm:

As to the views I hold on the effect of preoperative irradiation of cancer on the general tumour resistance of the patient and on the preoperative radiation technique I would like to refer to what I said on these questions before the Meeting of the Northern Association of Medical Radiology in Oslo 1939 (Nord. Med. 1940, Vol. 8, p. 2739) and at the meeting of the Swedish Medical Association on May 13 1941 (Trans. of the Swed. Med. Ass., Nord. Med. 1941, Vol. 12, p. 3435—36).

On this occasion I would only like to draw your attention to a state of affairs which, I think, at any rate to some extent, might explain the different results obtained by surgical treatment of cancer mammae in the hands of different surgeons, although in the main similar radical operations have been carried out.

I am referring to the very different way in which different surgeons consider the risk of cancer inoculation of the wound surfaces during actual operations.

For those who have seen how easy tumour inoculation may take place in animal experiments with a minimal quantity of tumorous fluid, it is clear there is considerable risk of tumour inoculation if a wound surface comes in touch with either instruments or fingers that have been in contact with cancer- or sarcoma tissues or with the cut surface of the tumour side of the operation wound. It would therefore seem an important part of the technique in operating for malignant growths, not only immediately to exchange instruments that have come in touch with tumorous tissue or fluid but also to keep away and in a suitable manner cover up the surfaces on the tumour side of the operation wound. It would seem that this rule should be heeded at least as much in operations on glandular regions as in operations for primary growths.

Dr. JENS NIELSEN, Copenhagen: *Indications and results in the roentgen treatment of cancer of the larynx and hypopharynx.* (Will be published in Acta Radiologica, Vol. XXIII, fasc. 2 & 3.)

Dr. S. MUSTAKALLIO, Helsingfors: *The results of roentgen treatment of cancer of the larynx and hypopharynx.*

The paper was cancelled as the writer was prevented from attending.

Prof. S. LOMHOLT, Copenhagen: *Treatment by carbon-arc light and a new alternating current lamp for the purpose.*

Discussion: P. JACOBY, S. LOMHOLT, P. JACOBY.

Dr. J. CHYDENIUS, Helsingfors: *Rectal reaction after radiation treatment of cancer of the uterus.*

Discussion: A. INGELMAN-SUNDBERG, Fr. VON BERGEN, J. J. CHYDENIUS, J. HEYMAN.

Dr. AXEL INGELMAN-SUNDBERG, Stockholm: The combined intracavity radium treatment of cancer of the uterus practised at the Gynecological Service of Radiumhemmet even since it was evolved by FORSSELL and HEYMAN, is very seldom attended by injuries to other parts of the intestine than the rectum. Only in the case of an intestinal loop being adherent to the pouch of Douglas or the uterus itself is there a risk of injuries to other parts of the intestine. Severe injuries are extremely unusual; a mild reaction in the rectum is sometimes found, however.

The subjective troubles are those generally characterizing proctitis, namely, straining at stool, the passage of mucus, difficulty in sitting, etc.

The symptoms come in one or more periods, during which they vary rather considerably from day to day. Proctitis, usually in a fairly mild from, occasionally appears three or four days after the treatment, but is of short duration. The main period of troubles generally comes about six months or, less often, one year after the treatment and lasts for one to six months. Any further periods are usually shorter and milder. The symptom which lasts the longest time — often for the rest of the patient's life — is rectal bleeding, generally in the form of blood-stained stools, in connection with constipation.

The most characteristic feature of the rectal reaction is its position at the level of the posterior fornix and practically always in the anterior wall of the rectum. Scarcely any changes can be palpated during the initial proctitis, with the possible exception of mild edema. Rectoscopy reveals an edematous and easily bleeding patch in the mucous membrane corresponding to the posterior fornix. More pronounced changes are present during the main reaction. The first change to be felt now is a fairly well circumscribed portion of the anterior wall of the rectum protruding into the lumen. This swelling, which is about 2 cm. in diameter and covered by thick, edematous, somewhat rough mucosa, is fixed and bleeds readily on palpation.

In some cases the edema disappears within a month or so, resulting in atrophy of the mucosa accompanied by the usual telangiectasis found in cutaneous reactions. In other cases an ulcer develops. In its typical form the rectal lesion following the application of radium is more or less oblong, often lies transversely and bears a lardy coating. It varies in extent from a pea-sized hollow to one measuring about 4 cm. in diameter. Occasionally the ulcer works downwards and may reach a depth of as much as one phalanx, in which case there is obviously a risk of perforation to the vagina.

In addition to the reaction in the mucosa, we find more or less pronounced swelling of the rectal wall and the periproctic connective tissue. At first this swelling is confined to the immediate neighborhood of the lesion. If the ulcer is large, the swelling gives it the appearance of a callous lesion which may be mistaken for cancer. Later the inflammatory swelling spreads out sideways in cords.

Small ulcers generally heal within a few months to one year. In exceptional cases a rectovaginal fistula develops, but these too usually close spontaneously.

The site of a healed rectal reaction is marked by an atrophic patch in the mucosa surrounded by telangiectatic vessels and drawn in and fixed to a transverse ridge or fold in the anterior rectal wall. This ridge continues in the shape of cords to one or both of the pelvic walls where it often ends in a pyramidal swelling; sometimes the cords spread out fanwise. A slight stenosis in the rectum is relatively common. Severe stenosis, on the other hand, is very rare.

The symptoms are not always borne out by the objective findings. Inversely, pronounced changes may be found without any subjective troubles worthy of note.

Of our 3,054 cases of cancer of the cervix treated during the years 1914 to 1936, 8.5 per cent showed rectal reactions. Cases with subjective troubles only and no palpable changes were also included in this calculation.

In the autumn of 1931 and the spring of 1932, a series of measurements of the radiation intensity at different levels in the rectum in connection with radium therapy were carried out. Sievert's condenser chambers, inserted one after another in a rubber tube which was introduced into the rectum, were used for the purpose. The measurements were made at the beginning of the treatment, two hours afterwards and, in some cases, also twenty-four hours later. The method was attended by various sources of error, particularly in view of the difficulty of keeping the tube in position. Despite this, it provided a good idea of the intensity of the radiation.

Altogether 19 cases of cancer of the uterus were submitted to measurement in connection with all the treatments. Further, all the patients lived more than one year after

the treatment, in other words long enough for any rectal reactions to have had time to appear. One case had to be excluded, since the measurement in the first treatment was very uncertain. Of the 18 remaining cases, 5 showed rectal reactions and 1 rectal troubles, which latter may well have been due to a cancer metastasis in the rectum. In all the cases the dose was calculated at every centimetre within an area of 3 to 17 cm. from the anus. The rectal reactions took place in the cases in which the largest dose was measured. The position of the latter in relation to the anus also corresponded well with the position of the rectal injury. Primarily, therefore, it seems that the cause of the rectal reaction should be sought in local overdosage. Individual sensitivity due to circulatory disturbances, etc. is probably a secondary consideration.

Dr. H. CHRISTIANSEN, Copenhagen: *Biopsy with revolving trephine: exploratory drilling.* (Published in Acta Radiologica, Vol. XXIII, fasc. 2).

Dr. OLOF SANDSTRÖM, Eskilstuna: *On direct focal dosage in teleroentgen therapy.*

Dr. JENS NIELSEN, Copenhagen: *Rotary irradiation.*

Dr. BRUNO JÄDERHOLM, Stockholm: *Photography of screen pictures.* (Published in Acta Radiologica, Vol. XXIII, fasc. 1)

Dr. O. AXÉN, Stockholm: *Screen photography of conscripts.*

Discussion: B. STRANDBERG, M. SIMON, O. SANDSTRÖM.

Dr. B. STRANDBERG, Stockholm: With reference to Dr. AXÉN's paper, I should like to give a short report on the results of the clinical examination we have made of the patients referred to the Military Hospital. Several regiments have sent most of the cases with pathological changes to us for examination. However, they have not done so consistently. For example, a few of the definitely tuberculous patients were sent directly to a sanatorium and a number of others with more uncertain and milder pathological changes were sent first to the roentgenological department at the Karolinska Hospital.

Thus far, 35 cases altogether have been referred to us. To obtain a better survey in my study of this material, I divided the cases into the two following groups, based on the results of the screen photography:

definitely tuberculous changes, but sometimes uncertain activity, and

parenchymal changes of uncertain nature, such as slight or atypical alterations.

I then re-divided the tuberculous group into cases with active tuberculosis, i. e. patients ill with tuberculosis, and cases with old, inactive changes. When judging the activity, I have taken into account the past history, the observations made on physical examination of the lungs, the temperature, the sedimentation rate, the roentgen picture and the presence of tubercle bacilli in the sputum or in the gastric rinsing fluid.

Of the 35 cases, 26 belong to the tuberculous group and the other 9 to the ones with processes of uncertain nature. Of the 26 tuberculous patients, 16 had active tuberculosis. Five of these 16 had open tuberculosis (bacilli in the sputum in 4 cases and in the gastric rinsing fluid in one). The remaining 10 had mild, probably old-standing, healed changes.

In the second group, the one with uncertain parenchymal changes of different nature, which included 9 cases, 3 patients had small, inactive tuberculous changes, 4 showed infiltrations of uncertain nature, perhaps of bronchopneumonic origin, and 2 were definitely non-tuberculous, one suffering from acute bronchopneumonia and the other from bronchiectasis.

Thus 29 out of 35 patients showed tuberculous changes. At least 16 of these 29 are ill in the real sense from tuberculosis and 5 showed tubercle bacilli.

Because of lack of space we have not been able to keep all these patients under observation for any length of time. A number of them are to come back for follow-up. There has not been time to see the results of guinea-pig tests and the like. It is possible, therefore, that the number of patients who must be considered ill or who show tubercle bacilli, will increase.

I have also gone through the cases with regard to heredity and past history. I found that of the 33 cases with changes almost exclusively of definitely tuberculous nature, only 3 had a tuberculous heredity and 9 a past history which might point to tuberculosis. Of the 16 cases of active tuberculosis, 3 had a tuberculous heredity and 5 a past history indicative of previous infection.

Considering the relatively limited material from which these tuberculous persons were taken, namely, apparently healthy military conscripts and others in the garrison of Stockholm, it is obvious that this method is one of valuable aid in the fight against tuberculosis.

Dr. M. SIMON, Stockholm: There are probably many of us who never, it is true, have to undertake such mass examinations as to justify the fitting up of an apparatus for screen photography but who nevertheless sometimes have to carry out »mass» examinations on a lesser scale, e. g. a few hundred subjects.

Thus a couple of years ago, at the request of the Board of Health, I undertook to examine about 700 employees in a semi-private enterprise. I then made use of a method which gave quite a satisfactory result but which proved far less expensive than all others — apart from screening alone which of course, at any rate so far, has not yet been generally considered fully satisfactory for the purpose.

The way I went about it was this that I took a photo on paper, 30×30 or 24×30, of all the patients after short screening in various directions. The paper photo proved to be well adapted to the object of picking out such suspicious cases requiring a closer examination. For such occasional group examinations, therefore, I should like to recommend this simple and inexpensive method.

Dr. OLOF SANDSTRÖM, Eskilstuna: In July 1939 I had the good fortune to follow, during one week, the so-called »Volksuntersuchung» with screen photography in Gau Mecklenburg in Germany, partly in the city of Schwerin where Professor HOLFELDER at that time worked under his SS roentgen standard, partly in Frankfurt a/M where the central bureau for development, examination and registration of the material was located. It was very interesting to make the acquaintance with all the exact details of the organisation. With 6 outfits — 2 of which in specially devised busses with a selected staff of 60 SS-men — HOLFELDER had had screen photoes taken of the population numbering about 1 million people in the course of 3 months. While I was there the frequency per day rose to 20,000 people! The small Leica films were sent to Frankfurt for development. 12 doctors in the town and surroundings examined during their spare time the rapid screen films and one of them could examine as many as 3,000 a day.

It was also interesting to note the intimate co-operation between the radiologists and the Health Ministerium of Mecklenburg (Head: Dr. PFREIMBTER). Suspicious cases were referred to Dr. PFREIMBTER and later thoroughly examined, clinically and roentgenologically.

I do not know anything about the ultimate result of the mass investigation in Mecklenburg. When I was there Prof. HOLFELDER had classified 366,000 roentgen examinations by the rapid method. The outcome of this was that in about 5,000 cases (1.37 %) active tuberculosis was suspected and that 500 cases (0.12 %) had obvious cavities (thus together 1.49 %). Five per cent of the examined persons showed healed changes in the form of calcifications and indurations. These mass examinations revealed among other things that the rate of disease was in some areas distinctly low while in others it was notably high. In one village one came across 20 fresh cases and at the same time the source of infection was discovered. This mass examination also gave good indications as to the frequency of other intrathoracic affections, such as miners' lung and pulmonary tumours. In Mecklenburg echinococcosis had an endemic character and in the above statistical account lung echinococcosis was found in 160 cases (0.04 %). An »Atlas of rapid screen

photography of the thoracic cavity» will be published shortly, by HOLFELDER and BERNER (Ed. by Thieme, Leipzig 1939) which should be in a good guide for judging the value of mass roentgen examinations by the present standard of technique.

The social organisation was also of great interest. It enabled as much as 98 per cent of the population to partake in the examination. That those examined has themselves to pay 50 pfennig for the examination was psychologically correct and made it possible to carry out the examination without any State contribution. The realisation of this, according to our standards, gigantic mass examination was also furthered by the ideal view taken of it by all helpers and facilitated by the understanding attitude of the population.

As to the most suitable film-size for these rapid screen photoes I am definitely of the opinion that the small size of 24×36 mm. is the correct one for such mass examinations, instead of the bigger size of 75×75 mm. as used by JANKER. It is only by using such dimensions of the film that the practical advantages of this screen-picture photography can be utilised. I hope that here in Sweden progress will unreservedly be in the direction of small-sized films. Even if their use is at present relatively limited, the rapid strides made in roentgen and film technique bring with it great possibilities for still further refinement.

Dr. NILS WESTERMARK, Stockholm: *On the circulation through the heart and lungs, simultaneously recorded by roengen-cinematography and electrocardiography.*

Discussion: SV. R. KJELLBERG, S. NYLIN, C. G. SUNDBERG, N. WESTERMARK.

Dr. GUNNAR JÖNSSON, Stockholm: *The roentgenographic diagnosis of pathologic conditions in the nasopharynx.* (Published in Acta Radiologica, Vol. XXII, fasc, 5—6.)

Discussion: E. BERVEN, P. FLEMMING-MOLLER.

Professor P. FLEMMING-MÖLLER, Copenhagen: Pointed out that tomographic sections through the nose and pharynx are a very valuable supplement to the roentgen diagnostics of naso-pharyngeal tumours which far more clearly than ordinary roentgen examination show the distribution of the tumour in relation to the surroundings; naturally, however, the sections must then be laid in the frontal as well as the sagital plane. The speaker had himself on two occasions had the experience of tumours in this region where tomography was a very valuable aid to the elucidation of the distribution and character of the growth.

In summary it may be said that tomography is a very valuable new asset to the roentgen diagnostics of diseases of the nose and its accessory sinuses which it is worth while to bear in mind. This has also been noted by others, particularly by American workers (SHERWOOD-MOORE), and our experiences from Rigshopitalet has shown the upper air passages with the nose and its surroundings to be the region where this special mode of examination yields good results.

Dr. BO STENSTRÖM, Stockholm: *A new bile contrast agent.*

Dr. NILS P. EDLING, Stockholm: *The interureteric torus in the roentgen picture.* (Published in Acta Radiologica, Vol. XXII, fasc. 5—6.)

Dr. ERIK LUNDSTRÖM, Stockholm: *Demonstration of a sluice device for wet films.* (Published in Acta Radiologica, Vol. XIII, fasc. 1.)

Dr. T. P. ROSENDAL, Copenhagen: *Case of multiple lung infiltrations.* (Published in Acta Radiologica, Vol. XXII, fasc. 2.)

Discussion: S. LOMHOLT, E. DE FINE LICHT, W. MAGNUSSON, P. FLEMMING-MØLLER, T. DALE, E. LINDGREN, T. P. ROSENDAL.

S. LOMHOLT, Copenhagen: It was interesting to hear Dr. R:s statement that even severe changes in the lungs in cases of Boeck's sarcoid may disappear spontaneously in

a relatively short time. In the Skin Department of the Finsen Institute we have surely a greater number of patients with Boeck's sarcoid than in any other clinic, more than 120 cases. Many of these patients have been followed year after year, even from one decade till another but in none of them have I seen described complete disappearance of more massive changes, especially not of the strange ramificating design referring to fibrous strands branching out from the hilum. It would be very interesting to hear the views held by the experienced radiologists present on this matter. We have always looked upon these changes as characteristic and permanent.

At the same time I would like to say that in dermatological circles we have let fall the barriers between the four clinical conditions mentioned here: Boeck's sarcoid, Lupus pernio (BESNIER), Febris uveo-paratoidea (HEERFORDT) and Ostitis cystica (JÜNGLING). As to the last condition I would rather like to point out here in Stockholm that the first clear description of these bony changes is credited Dr. JÖRGEN SCHAUMANN in a work to the French Dermatological Society in 1914 for which he obtained the Zambaco price. Furthermore the latest investigations seem to indicate that the term »tuberculosa» as an expression of tuberculous etiology had better be discarded for these conditions, in that Dr. KVEIM, a Norwegian worker, has shown that in these conditions a specific cutaneous reaction can be obtained by injecting an extract from a lymphnode taken from a patient with an active Boeck's sarcoid — a term, besides, which we now prefer to exchange for the more rational name of Lymphogranulomatosis benigna, as suggested by SCHAUMANN.

Dr. PUTKONEN, a Finnish colleague, has been carrying out a great many systematic examinations with our material in the course of the last five months and thus found the reaction to be positive in the great majority of patients with benign lymphogranulomatosis and practically speaking in all those with an active form of the disease. On the other hand it was found negative in all the many control cases tested, of which there were many patients with lupus. We thus maintain that the long discussion regarding the etiology of the disease has been definitely settled, i. e. that it is a disease »sui generis». Already earlier there were of course many factors against the assumption of a tuberculous origin.

Dr. E. DE FINE LICHT, Hellerup: Dr. ROSENDAL's paper prompts me to draw attention to the fact that in some cases we are able to differentiate a group with congenital (?) cystic bronchiectasis[1] from the other cases by the aid of tomography. Six months ago I had a patient with the signs of lung fibrosis where tomography revealed the undoubted presence of several cavities. The patient died and autopsy verified the diagnosis of bronchiectatic cysts. Cases of this kind with well marked fibrosis are rare and the above case will be published elsewhere.

Dr. FLEMMING MØLLER, Copenhagen: Mentioned in reference to LOMHOLT's statements that pulmonary changes in BOECK's sarcoid may so completely disappear as to make it impossible to detect any earlier signs of infiltration, even such of severe nature.

Prof. T. DALE, Oslo: It is not rare for multiple lung changes in Boeck's sarcoid to show retrogression. In Norway Dr. KVEIM in the Skin Department of Rigshospitalet has worked out a specific cutaneous reaction which seems to be reliable in cases of Boeck's sarcoid. By reason of this I have after-examined a number of old cases, all from Prof. BOECK's time, and among other observations I have also had occasion to notice retrogression of lung changes, where present.

Dr. ERIK LINDGREN, Stockholm: At the Roentgen Department of the Seraphimer Hospital we have not had the opportunity of observing any greater number of benign lymphogranuloma, only some ten cases during the last five years. Seven have been followed more closely by control- and after-examinations. Four of these cases proved on exa-

[1] P. S. The case is identical with that recently published under the name of Tuberous Sclerosis by BERG and ZACHRISON in Acta Radiol. Vol. XXII, Fasc. 3 p. 425.

mination to be subjectively and clinically quite well, earlier roentgenological changes had quite disappeared; in one case the changes were pertly retained but had diminished, in two cases they were about the same as before. According to our experience, therefore, we may find complete disappearance without any subsequent traces, not only of such changes that depend upon atelectasis but also of enlarged hilum glands and those distinct small mottled changes found in the lungs. In two cases such disappearance took place in less than twelve months.

Dr. T. P. ROSENDAL: In illustration of how frequently it happens that pulmonary changes clear up in cases of Boeck's sarcoid I would like to refer Prof. LOMHOLT to an article in »Ergebnisse des ges. Tub. forsch.» IX, 1, 1939 where LEO HANTSCHMANN is recording 7 cases, with complete disappearance of the lung changes in one case and partial disappearance in another. I would further inform you that Dr. BONDO GRAVESEN will shortly include a description also of this item in a more extensive publication on pulmonary changes in Boeck's sarcoid.

Dr. ERIK MOBERG, Stockholm: *The corticalis osteoid, a type of localised skeletal change, of interest from the point of view of differential diagnosis,*

Dr. J. FRIMANN-DAHL, Oslo: *Experiences of roentgen findings in intestinal knots.* The paper was cancelled as the writer was prevented from attending.

(Published in Acta Radiologica, Vol. XXIII, fasc. 2.)

Dr. ERIK LYSHOLM, Stockholm: *Cerebral angiography.*

Dr. KNUT LINDBLOM, Stockholm: *Contrast examination of the epidural space.*

Professor NILS ANTONI, Stockholm:

a) *Displacement of cerebral parts beyond capsular borders (falx, tentorium, foramen magnum) and its bearing on the ventriculogram.*

b) *Subdural encephalography through cisternal puncture.*

Discussion: ERIK LINDGREN, ERIK LYSHOLM, ERIK LINDGREN.

Dr. ERIK LINDGREN: The radiological examination of the subdural space is not an easy one. To obtain a tolerably reliable result of the examination we must have an air quantity large enough to free the brain surface from the skull-cap to a sufficient extent. Preferably the air layer should have a depth of 8—10 millimeter in an antero-posterior picture with the patient in sitting position. This will cause sufficient depression of the brain so that adhesions, if present, will be stretched and thus more readily detected. The aim of the examination is to cause the injected air to shift about by altering the position of the patient's head, causing by rotation different parts of the brain surface to be explored. In every position frontal as well as lateral pictures should be taken. A small quantity of air has also the drawback of claiming the position to be frequently altered: the examination takes a longer time and becomes more troublesome to the patient, more films are required. The finding out whether adhesions are present or not is rendered more difficult if the subdural space normally is not free but transversed by Pacchionian granulations and vessels which in different patients may vary considerably in extent and position. Nearer the superior longitudinal sinus there are always Pacchionian granulations which to some extent fix the brain toward the midline wherefore the air layer here normally is never so high as further down over the convexity. At the beginning of the examination there is at times no air at all along the superior longitudinal sinus over an area measuring 1 or more cm. in breadth. In such cases, however, it is possible by suitable turns of the head of a sitting patient, to force the air in between the different granulations; the anatomical data then appear more distinctly. It is impossible to distinguish between adhesions lying close to the midline and Pacchonian granulations. To be able to say that strands transversing the subdural space are due to pathological conditions they must

extend further down on the convexity than the Pacchionian granulations do or be located in such places where granulations are never to be seen. Solitary small vessels may however transverse the subdural space even low down on the convexity. These vessels are thin, regular chords with a tent-shaped foot on the brain surface which are there tangentially struck by the roentgen rays. This is probably so explained that on the subdural space being filled with air the vessel becomes stretched; the arachnoid thereby becomes lifted up a wee bit just where it is pierced by the vessel. Such vessels differ from adhesions in this respect that, according to our present experience, the latter are never so regular and thin as the vessels. Lateral pictures often yield less results in the case of adhesions highly situated than would perhaps a priori be expected because of the fact that they are projected against the falx. On the whole one is not justified in diagnosing adhesion, even in the case of a very broad strand visible in a lateral picture, unless it can be so clearly localised in an anteroposterior view that extensive Pacchionian granulations can clearly be ruled out. (In reference to this radiograms were demonstrated for elucidation of the normal anatomy as well as pathological conditions with attention being drawn to difficulties in the differential diagnosis).

Dr. FOLKE KNUTSSON, Stockholm: *Experiences with epidural contrast investigation of the lumbo-sacral canal in disc prolapse* (*perabrodil*). (Published in Acta Radiologica, Vol. XXII, fasc. 5—6.)

Discussion: T. GORDH, K. LINDBLOM, E. LINDGREN, K. LINDBLOM, E. LINDGREN.

Dr. T. GORDH: The epidural injections just discussed are performed as a typical sacral anesthesia, which is an epidural anesthesthesia as well. But in investigating segments in the thoracal and upper lumbar regions you may use the technique of the extradural or epidural anesthesia. This method is more complicated than the sacral way and the difficulty is to estimate when the tip of the needle has reached the epidural space between ligamentum flavum and the dura. This space occupies a space of one to three millimeters and is more pronounced in its dorsal portion. Various techniques are devised to reach this space. The negative pressure technique, first introduced by GUTIERREZ, is based on the fact that a negative pressure exists in the epidural space. To the needle is attached a small U-shaped water manometer or as we do a hanging drop is placed in the end of the needle. The puncture is made as a spinal puncture and when the tip of the needle penetrates into the epidural space the manometer at once shows the negative pressure or the hanging drop will be sucked in.

Another method used by DOGLIOTTI is as follows. The needle is inserted through the interspinous ligament, care beeing taken to remain in the midline. When the tip of the needle reaches the ligamentum flavum a marked resistens is felt. It is necessary at this point to stop the advance of the needle. The stylet is removed from the needle, which is now connected with a syringe containing 5 cc of normal saline solution. With a pressure exerred on the plunger the needle is slowly pushed into the depth of the tissue. The resistance to the injection is now marked. As soon as the tip has penetrated the ligamentum glavum the resistance disappears and the solution escapes very rapidly and freely into the epidural space. Before further injection with the anesthetic solution one must assure that the needle has not penetrated the dura. If there is escape of blood or spinal fluid it is advisable to withdraw and re-insert the needle in another space.

We have successfully done extradural injections with a mixture of a 2 % novocain solution and Perabrodil. Roentgenograms have shown the diffusion in the epidural space and along nerve roots very dinstinctly.

Dr. ERIK LINDGREN: Our chance of demonstrating disc prolapse by myelography through contrast medium injected into the subarachnoidal space depends upon whether

the prolapse is large enough to cause deformation of the subarachnoidal space. At the Seraphimer Hospital we have therefore also tried with positive contrast epidurally with the hope thereby to find small protrusions. The contrast has been injected into the sacral canal but in some cases we have also made use of a way of puncture suggested by DOGLIOTTI for use in a certain mode of anaesthesia. By such means the contrast can be injected near the level of the supposed-to-be pathological process. We have as yet no greater experience of the method in question, only some ten cases having been so examined It would seem, however, as if the method had a very great drawback in that one has no possibility in controlling the spread of the injected fluid. Immediately after the injection the contrast spreads over very large areas if the patient occupies a horisontal position during the injection; slight raising or lowering of the head or foot does not alter this condition. Part of the contrast medium passes through the foramina intervertebralia but judging by our present experience we are not justified in assuming at once some pathological process, should the contrast fail to pass out via some foramen. Up to the present we have not had the chance of examining any disc prolapse. Oh the other hand we have had a case of extradural tumour which caused some obstruction. Close to the obstruction we could see small irregular filling defects in the contrast medium. The same tumour could also be seen by gas myelography.

It must be emphasized in this relation that in lateral pictures we may often notice a bulging posteriorly of one or more intervertebral discs without there being any proper prolapse. This would particularly seem to be the case in elderly persons but may also occur in young people. From what has been said here to-day it appears as if this state of affairs is not generally known.

In illustration of what had been said above radiograms were shown. A couple of pictures were further shown of contrast injection into nucl. pulposus in living subjects. The contrast medium spreads in the nucl. pulposus but cannot be seen round about. As can be expected absorption is poor. Still after 4 hours the contrast has scarcely diminished. The demonstrated pictures of contrast injected into the nucl. pulposus are to be regarded as a curiosity and are by no means intended to suggest any kind of new method. Puncturing and injection of the contrast have been done during screening with the needle inserted at an angle of about 45° to the spine.

Dr. H. REITAN, Oslo: *Movements of fluid inside the cerebro-spinal space.* The paper was read by Prof. T. DALE. (Published in Acta Radiologica, Vol. XXII, fasc. 5—6.)

Discussion: P. JACOBY.

Dr. Bo MARKMAN, Stockholm: *Special table for myelography.*

Discussion: T. DALE, Oslo: Pohl's omniscope can be used for examinations of the kind mentioned by the speaker.

Dr. ERIK LINDGREN, Stockholm: *Demonstration of apparatus for localising foreign bodies in the eye.*

Discussion: S. RIBBING, G. RUNSTRÖM, E. LINDGREN, S. RIBBING, E. LINDGREN, S. RIBBING, K. LINDBLOM.

Dr. S. RIBBING: As radiologist to the Finnish Ambulance of the Swedish Red Cross I came in touch, last winter, with intraocular metallic splinters under *war conditions.* And though it was satisfactory to note that our Swedish field roentgen apparatus of the bigger type came up to expectations in every other respect, it was found necessary to adopt special supplementary arrangements for localisation of eye splinters. I had the pleasure of working together with my Finnish ophthalmological colleague, Dr. STENIUS, and we devised a localising apparatus chiefly in accordance with

COMBERG's method. The idea of this is to take films of the eye in a sagittal and frontal direction after having put a contact glass on it including four lead indicators fused with it in such a way that the indicators come to correspond to the position of limbus cornae. By these pictures we thus obtain the meridian on which the splinter is located, its distance from the sagittal axis of the eye and its distance the limbus cornae. The figures obtained are marked down on a chart (COMBERG) and I have been told that such a chart is the best possible guide for the operator for finding the splinter. The method was often supplemented by studying the movement of the splinter on varying the gaze, chiefly carried out according to AHLBOM.

On my return from Finland I was encouraged by Professor PLOMAN to continue taking an interest in these questions on behalf of the Board of Health and the outcome of this was that by the intermediary of Prof. PLOMAN I was charged by the Chief of the

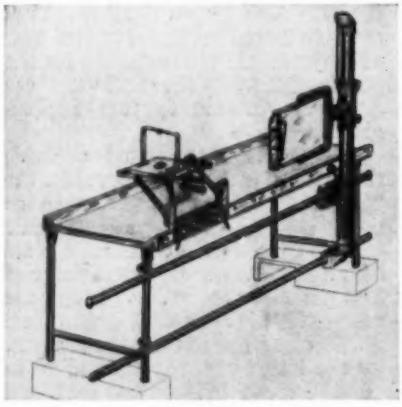

Fig. 1.

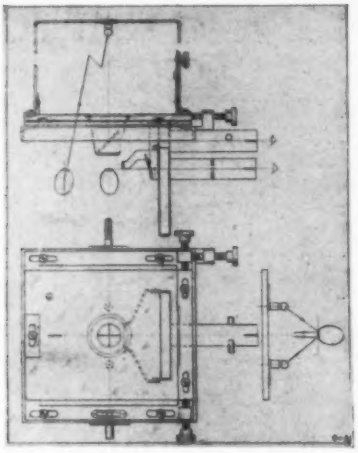

Fig. 2.

Army Medical Corps with devising a localising apparatus for field hospitals. Naturally I again sought the co-operation with Dr. STENIUS with the result that we have now jointly suggested an apparatus of which, for the time being, I am only able to show the mechanical drawings, carried out by Mr. LENNING of the firm GEORG SCHÖNANDER.

The basal claim here was an apparatus easy of transport and adaptable to a bigger field roentgen but also to practically all other roentgen outfits. Our joint experience had told us that one must be able to carry out an exact localisation even without any contact glass which for several reasons is often is unpractical. Furthermore, the localisation must be carried out with the patient in the supine position, the only position which a war wounded with an eye injury is likely to be able to manage. Above all must the method be good enough for localisation in the only seeing eye but one should also be able to use the sound eye as an aid to fixation. And it must also be possible to carry out localisation in the case of complete blindness. These are big claims but justified by our war experiences.

In the fig. 1 the apparatus is seen included in the field roentgen table. The patient is imagined lying with his head toward this end for localisation in the right eye and toward

the further end for localisation in the left eye. The central ray is adjusted by screening both for the vertical projection with the tube in trochoscopic position and for the horisontal projection with the tube at the side of the table. The patient's head is fixed by sand bags and is kept still during the whole examination. Particular arrangements have been adopted in order to secure complete and exact adjustment of the apparatus.

Fig. 2 shows a removable frame for the fixation lamp for the sound eye. The frame can be tilted along a protractor and the lamp can be moved across. The tilting is intended for the double-exposed lateral picture with change of gaze between the exposures. By three screws the centre of the apparatus is finely adjusted over the centre of the pupil while the operator is looking through the upper ocular. Further there are two small lamps emitting a light toward the eye, causing a couple of images in the cornea. When the central hair-cross is found right between these two images then the iris plane is standing horisontal. In the lower ocular the height of the apparatus is so adjusted that a small metal rod seems to touch the corneal vertex. This rod is included in the exposure for the profile picture. In the small "cup" the four lead points are seen fused in plexiglass.

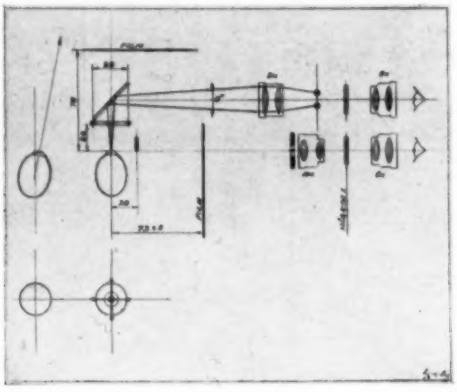

Fig. 3.

If no fixing sound eye is available the diseased eye has to be used for the purpose. To this end there are in the upper ocular (fig. 3) two small points of light which to the examined eye are seen to be at an angular distance of 8° from one another. By letting the patient fix his eye right between these points or at one of them, we are able, by the latter method, at any rate to some extent, to correct the gamma angle, i. e. the angle between the optic and anatomical axes of the eye.

In the case of a totally blind patient we have to make up for the fixation lamp by carrying his own index finger to the point he is to fix with his eye and in such cases, as is evident from the drawings, we are able to check up the fixation in the upper ocular during the very exposure. Three pictures are taken, 9 × 12 cm., one frontal in accordance with COMBERG's method and, similarly, one lateral but with this difference that the distance of the splinter is taken from the metal rod instead of from the lead points of the contact glass. The third picture is a side-view after shifting the gaze 30°.

I have been unable to enter into all the details of our device but STENIUS and I will return to the question in a joint publication. Finally I would add that we have tried by every means to construct an apparatus, easy to handle, and instructions will follow with it, clear enough to permit a radiologist, even totally inexperienced in the eye-splinter problem, to make a fully exact localisation even at his first attempt. If he fails, the fault is ours, not his.

Dr. FOLKE KNUTSSON, Stockholm: *The roentgenology of the femoro-patellar articulation.* (Published in Acta Radiologica, Vol. XXII, fasc. 3.)

The following delegates were invited to speak on the below-mentioned subjects:

Dr. Bo CARSTENSEN, Sandsträsk, Sweden: *Diagnosis and clinical features of pulmonary echinococcosis.*

Dr. KNUT LINDBLOM, Stockholm: *Arthrography of the knee-joint.*

Dr. SVEN R. KJELLBERG, Stockholm: *Salpingo-pelvigraphy.*

Dr. ERIK LINDGREN, Stockholm: *Air Myelography.*

On conclusion of the scientific proceedings the delegates were invited to visit the Roentgen-Diagnostic Departments of the Karolinska Sjukhuset and the Jubilee Clinic of King Gustaf V.

NORDISK FÖRENING

FÖR

MEDICINSK RADIOLOGI

avhåller sitt 12:te möte i Lund

den 20-21 juni

1942.

Föredrag anmälas till föreningens President Professor Lars Edling, Lund. Det är styrelsens varma förhoppning om ett talrikt deltagande i kongressen från de nordiska brödraländerna.

STYRELSEN